

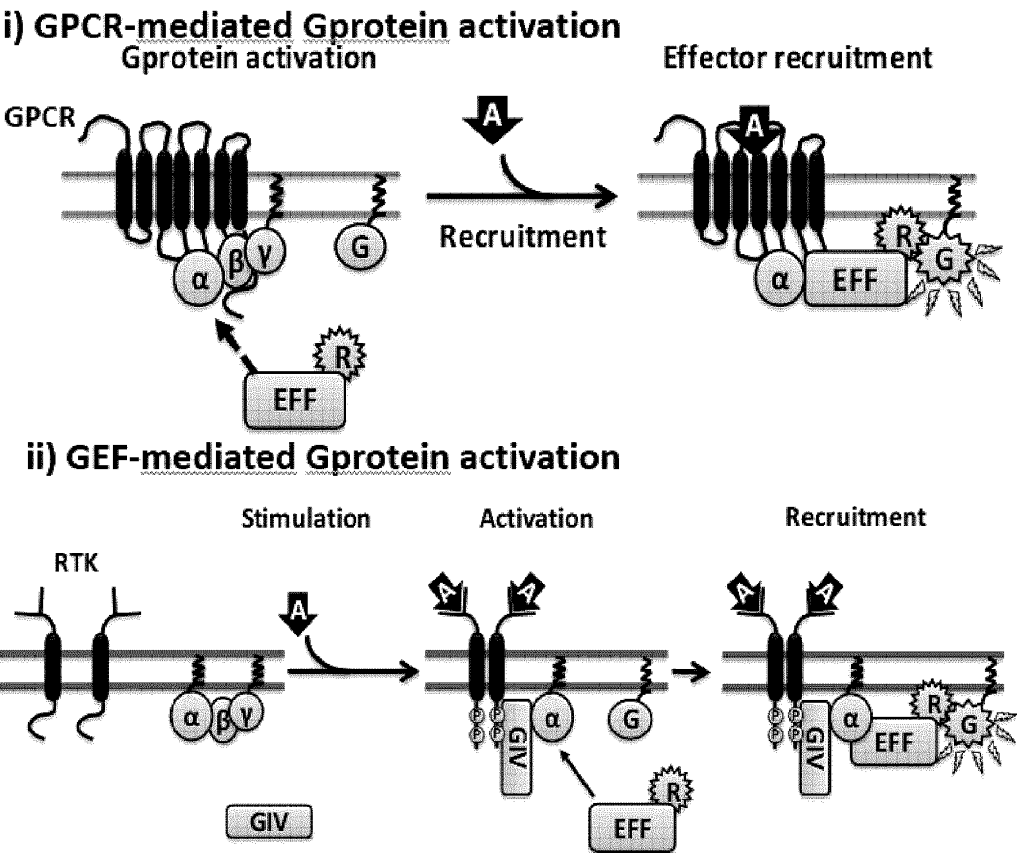


FIG. 1A

DRC:PAF/PAFR, RAP1GAP(SSS-AAA) sensor

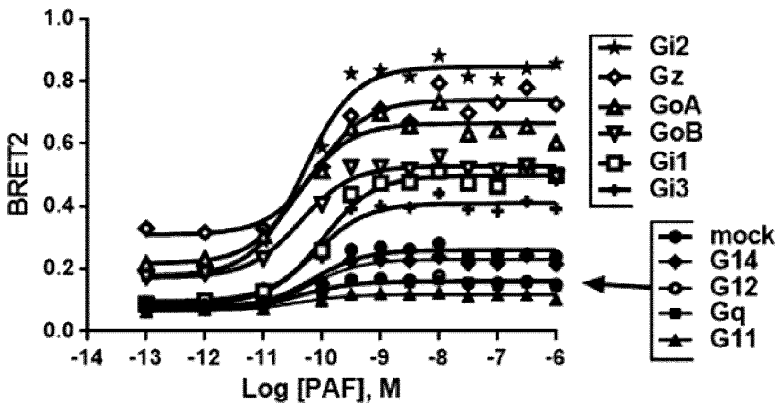


FIG. 1B

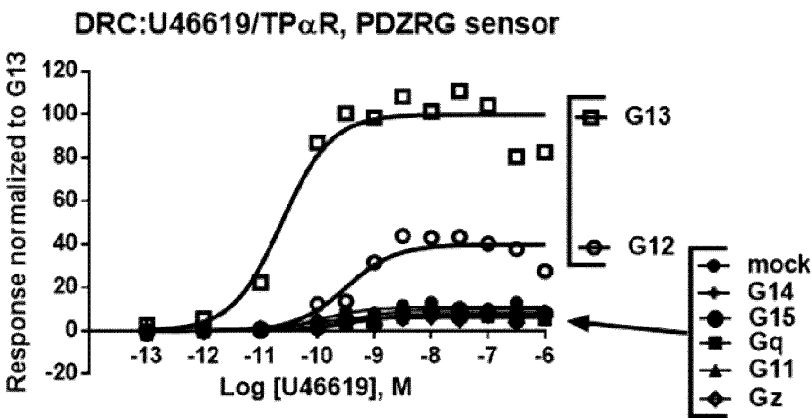


FIG. 1C

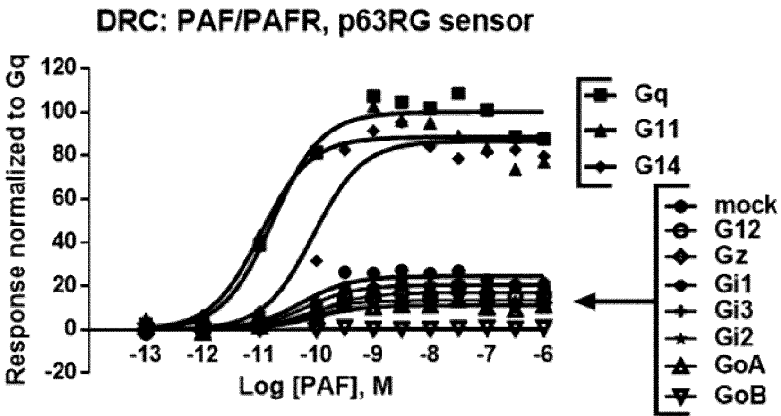


FIG. 1D

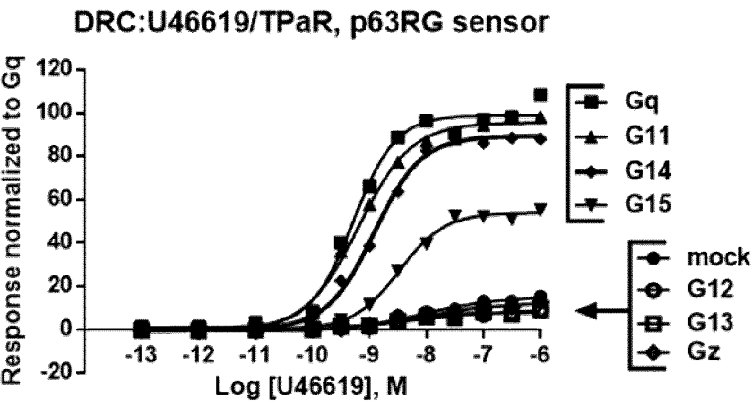
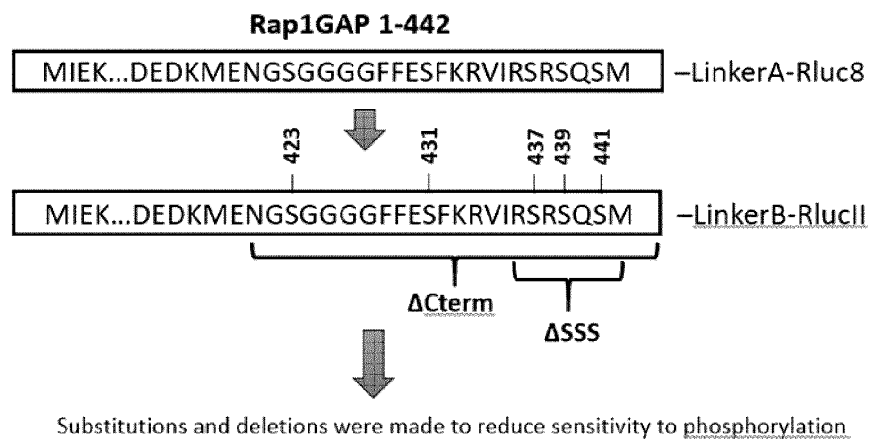


FIG. 1E

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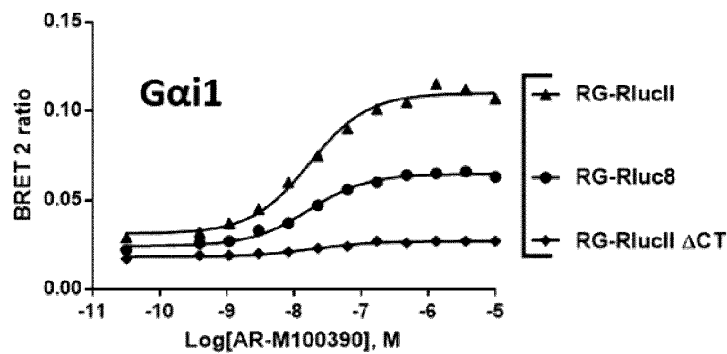
- Mutants**
- Rap1GAP $\Delta Cterm$ (=1-420)
 - Rap1GAP ΔSSS (=1-436)
 - Rap1GAP SS-AA (=S437A/S441A)
 - Rap1GAP SS-DA (=S437D/S441A)
 - Rap1GAP SS-AD(=S437A/S441D)
 - Rap1GAP SS-DD (=S437D/S441D)
 - Rap1GAP SSS-AAA (=S437A/S439A/S441A)
 - Rap1GAP SSS-TTT (=S437T/S439T/S441T)

LinkerA=GSGGGSGGGA

LinkerB=GSAGTGGRAIDIKLPAT

FIG. 2A

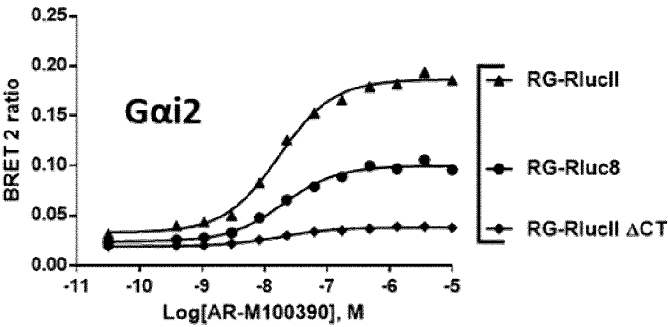
DRC hMOR1/ARM: Rap1GAP-Rluc +Gαi1/rGFP-CAAX



	Rluc8	RlucII	RlucII ΔCT
EC50	1.671e-008	1.696e-008	1.846e-008

FIG. 2B

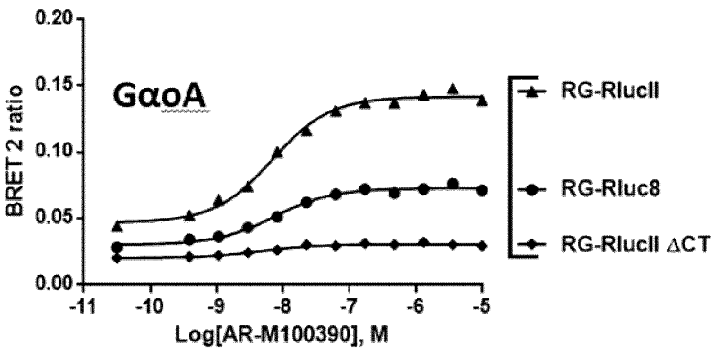
DRC hMOR1/ARM: Rap1GAP-Rluc +Gαi2/rGFP-CAAX



	Rluc8	RlucII	RlucII ΔCT
EC50	1.981e-008	1.693e-008	1.739e-008

FIG. 2C

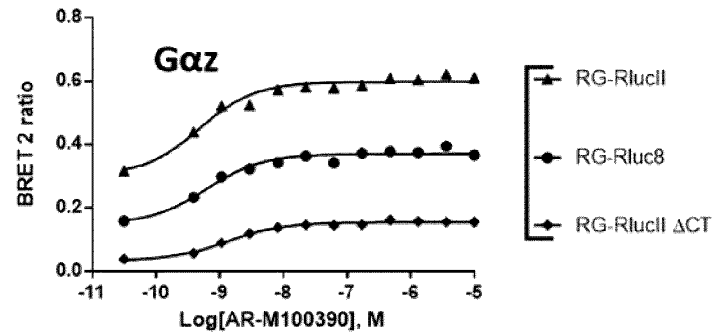
DRC hMOR1/ARM: Rap1GAP-Rluc +GαoA/rGFP-CAAX



	Rluc8	RlucII	RlucII ΔCT
EC50	7.442e-009	6.936e-009	4.671e-009

FIG. 2D

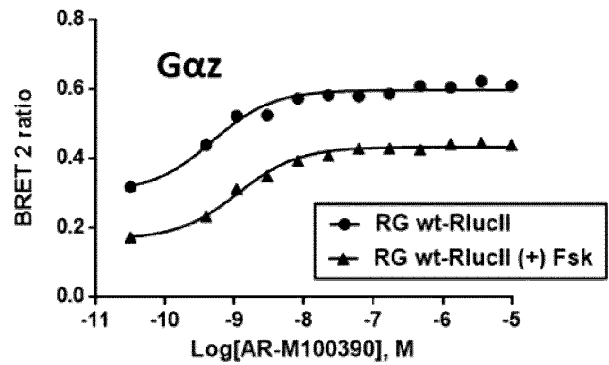
DRC hMOR1/ARM: Rap1GAP-Rluc +Gαz/rGFP-CAAX



	Rluc8	RlucII	RlucII ΔCT
EC50	6.273e-010	4.825e-010	1.328e-009

FIG. 2E

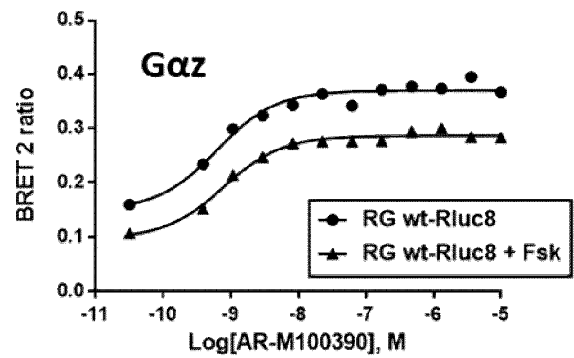
DRC hMOR1/ARM: Rap1GAP-RlucII +Gαz/rGFP-CAAX



	RlucII (-) Fsk	RlucII (+) Fsk
EC50	4.825e-010	1.123e-009

FIG. 2F

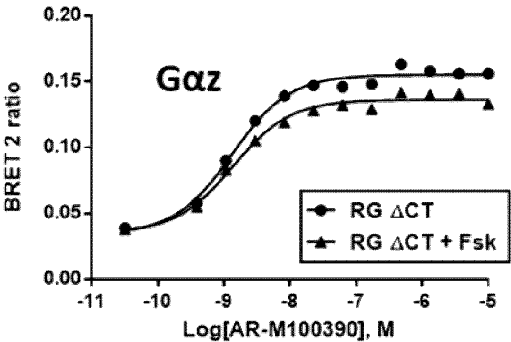
DRC hMOR1/ARM: Rap1GAP-Rluc8 +Gαz/rGFP-CAAX



	Rluc8 (-) Fsk	Rluc8 (+) Fsk
EC50	6.273e-010	7.811e-010

FIG. 2G

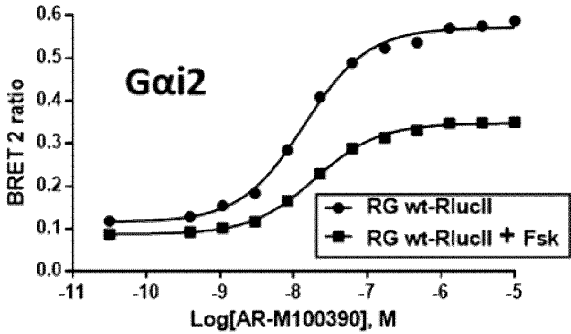
DRC hMOR1/ARM: Rap1GAP mut-RlucII +Gz/rGFP-CAAX



	RlucII ΔCT(-) Fsk	RlucII ΔCT(+) Fsk
EC50	1.328e-009	1.369e-009

FIG. 2H

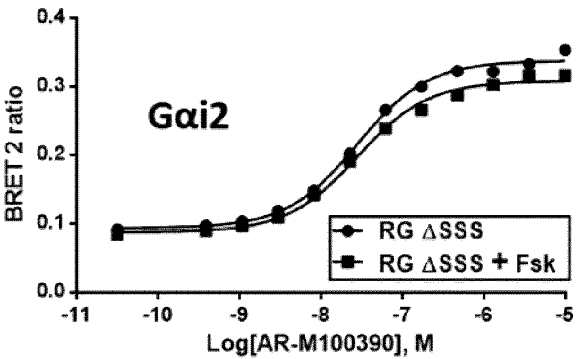
DRC hMOR1/ARM: Rap1GAP-RlucII +Gαi2/rGFP-CAAX



	wt (-) Fsk	wt (+) Fsk
EC50	1.389e-008	1.934e-008

FIG. 2I

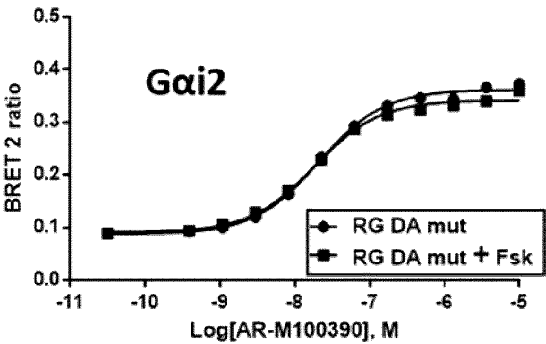
DRC hMOR1/ARM: Rap1GAP mut-RlucII +Gαi2/rGFP-CAAX



	ΔSSS mutant (-) Fsk	ΔSSS mutant (+) Fsk
EC50	2.798e-008	2.819e-008

FIG. 2J

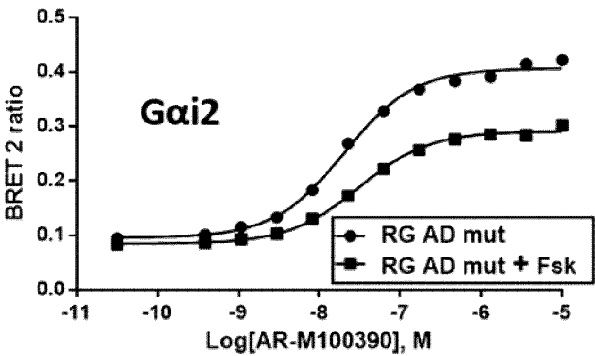
DRC hMOR1/ARM: Rap1GAP mut-RlucII +Gαi2/rGFP-CAAX



	DA mutant (-) Fsk	DA mutant (+) Fsk
EC50	2.088e-008	1.829e-008

FIG. 2K

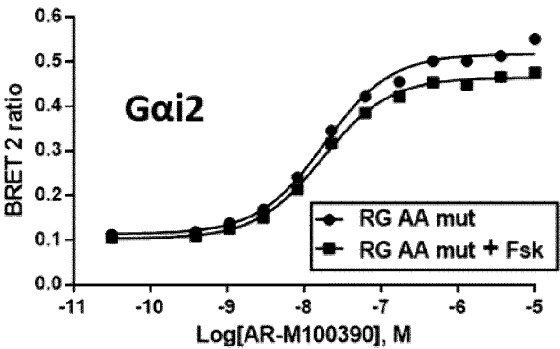
DRC hMOR1/ARM: Rap1GAP mut-RlucII +Gαi2/rGFP-CAAX



	AD mutant (-) Fsk	AD mutant (+) Fsk
EC50	2.023e-008	3.082e-008

FIG. 2L

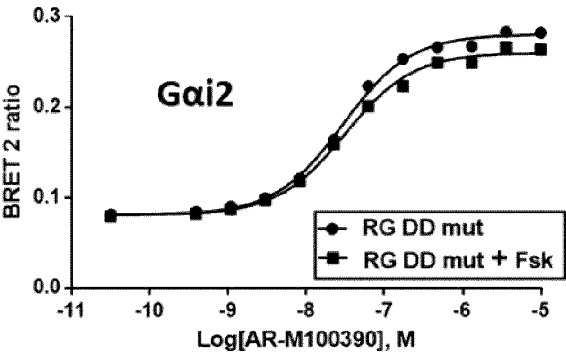
DRC hMOR1/ARM: Rap1GAP mut-RlucII +Gαi2/rGFP-CAAX



	AA mutant (-) Fsk	AA mutant (+) Fsk
EC50	1.841e-008	1.737e-008

FIG. 2M

DRC hMOR1/ARM: Rap1GAP mut-RlucII +Gαi2/rGFP-CAAX



	DD mutant (-) Fsk	DD mutant (+) Fsk
EC50	2.930e-008	3.145e-008

FIG. 2N

DRC hDOR/SNC80: Rap1GAP-RlucII vs GαoB/rGFP-CAAX

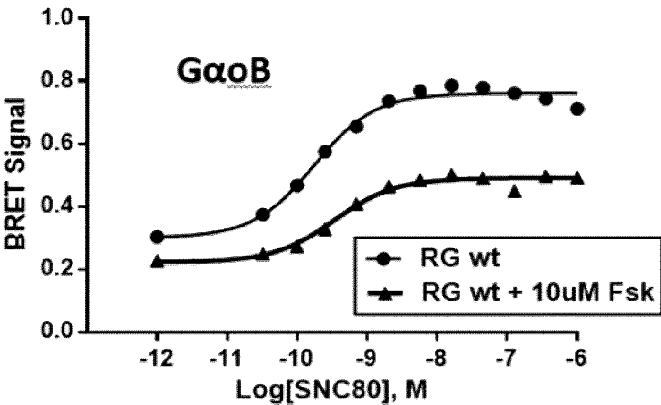


FIG. 2O

DRC hDOR/SNC80: Rap1GAP-RlucII vs GαoB/rGFP-CAAX

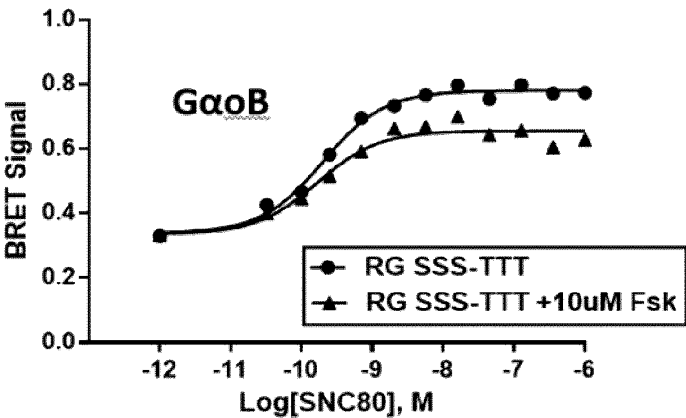


FIG. 2P

DRC hDOR/SNC80: Rap1GAP-RlucII vs GαoB/rGFP-CAAX

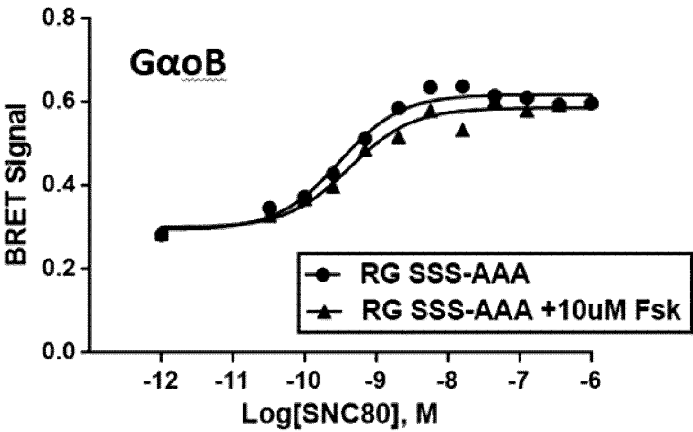
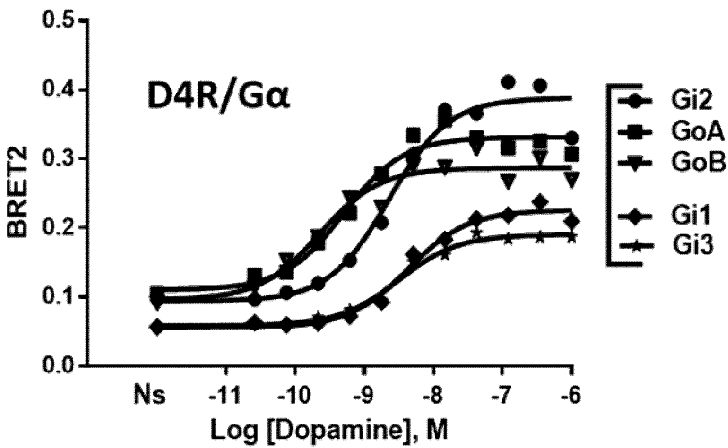


FIG. 2Q

DRC D4R, RAPGAP (SSS-AAA)-RlucII vs Gα/rGFP-CAAX



	GoA	GoB	Gi1	Gi2	Gi3
LogEC50	-9.300	-9.651	-8.365	-8.647	-8.505

FIG. 2R

DRC D4R, RAPGAP (SSS-AAA)-RlucII vs Gαz/rGFP-CAAX

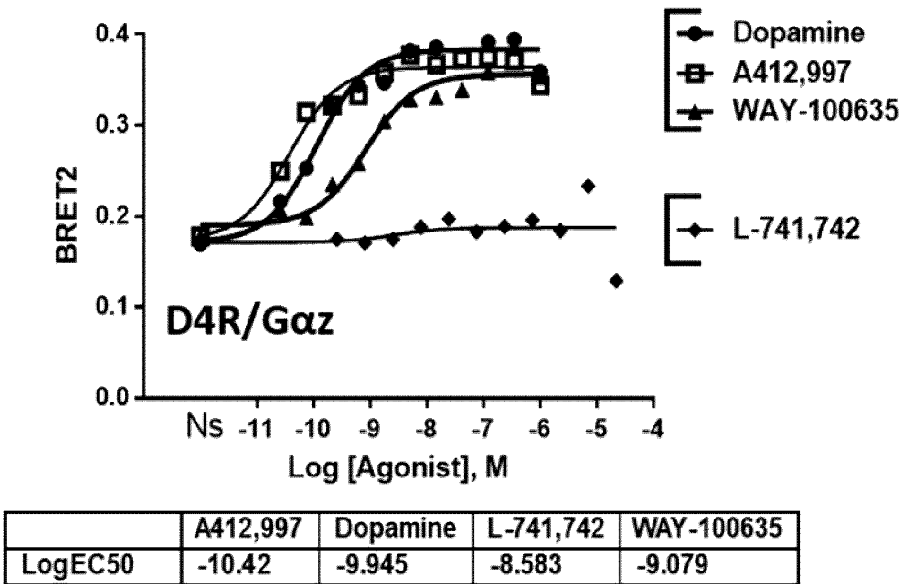


FIG. 2S

DRC D1R, RAPGAP (SSS-AAA)-RlucII vs Gαz/rGFP-CAAX

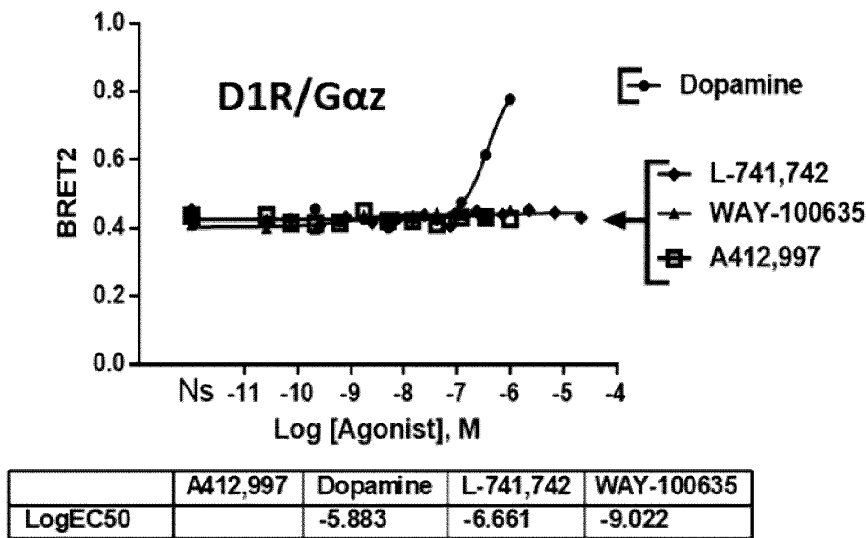


FIG. 2T

DRC D2R, RAPGAP (SSS-AAA)-RlucII vs $G\alpha z$ /rGFP-CAAX

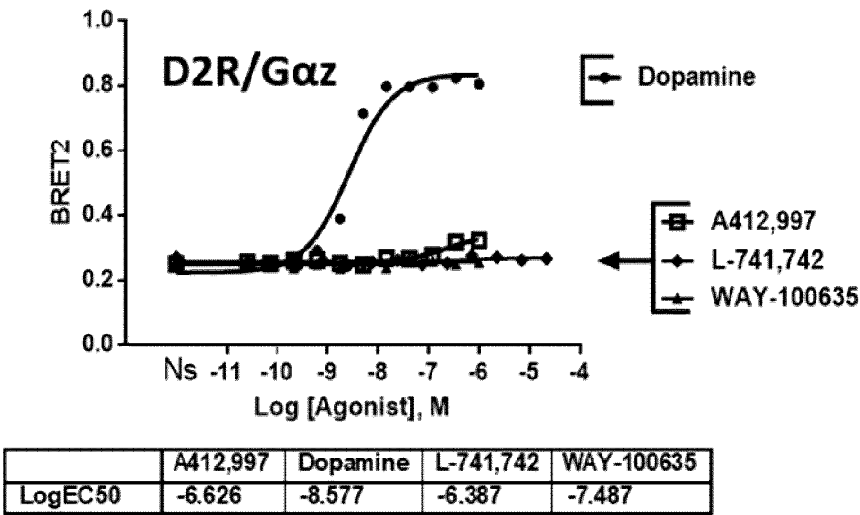


FIG. 2U

DRC D3R, RAPGAP (SSS-AAA)-RlucII vs $G\alpha z$ /rGFP-CAAX

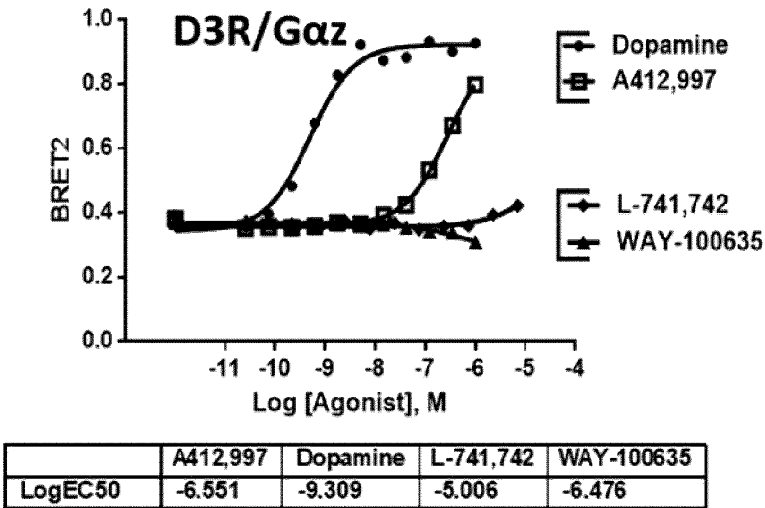


FIG. 2V

DRC D5R, RAPGAP (SSS-AAA)-RlucII vs Gαz/rGFP-CAAX

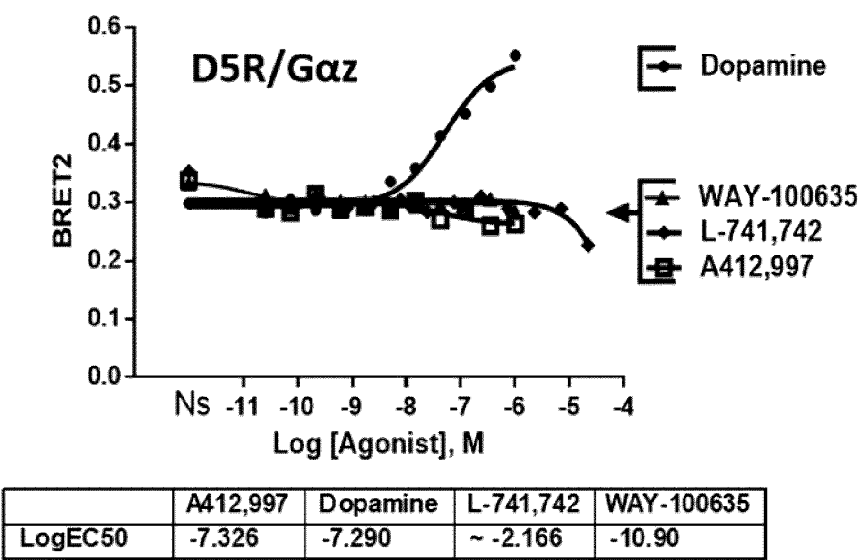


FIG. 2W

Z' factor: D4R, Rap1GAP (SSS-AAA)/Gi2 sensor

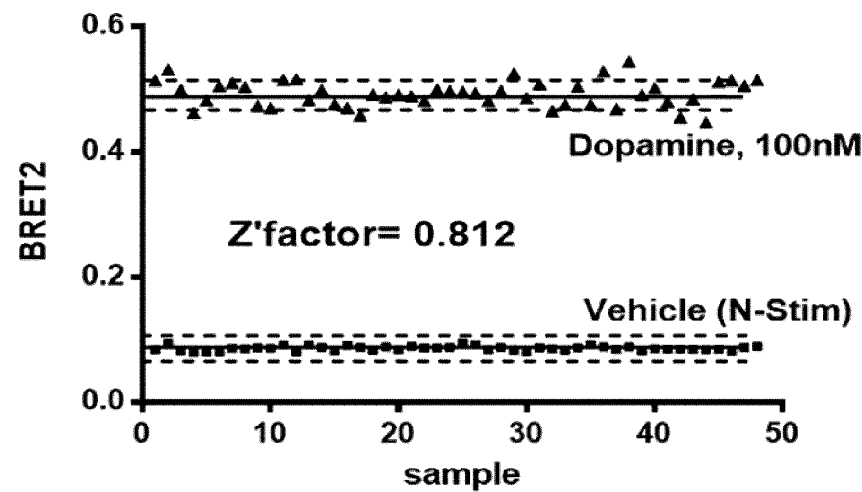


FIG. 2X

Z' factor: D4R, Rap1GAP (SSS-AAA)/GoA sensor

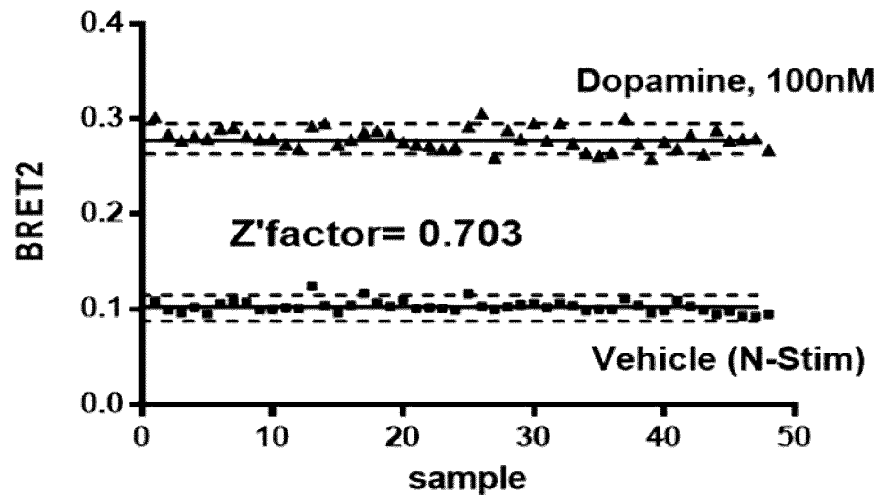


FIG. 2Y

Z' factor: D4R, Rap1GAP (SSS-AAA)/Gz sensor

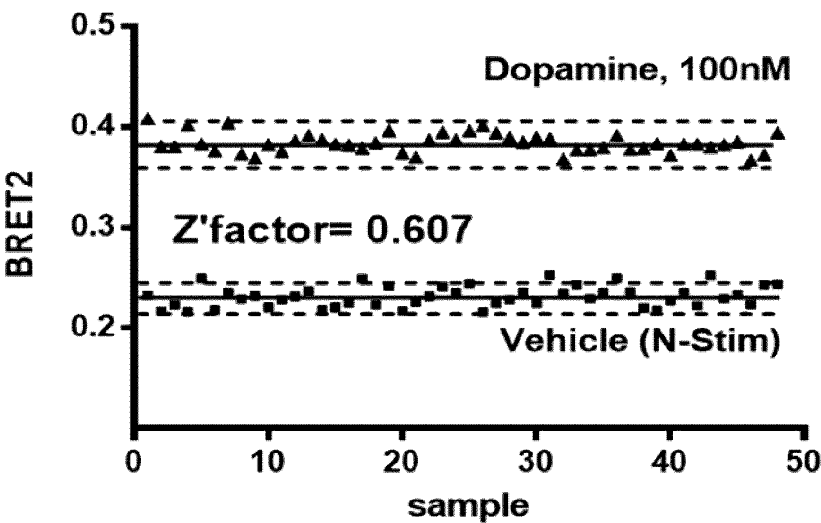
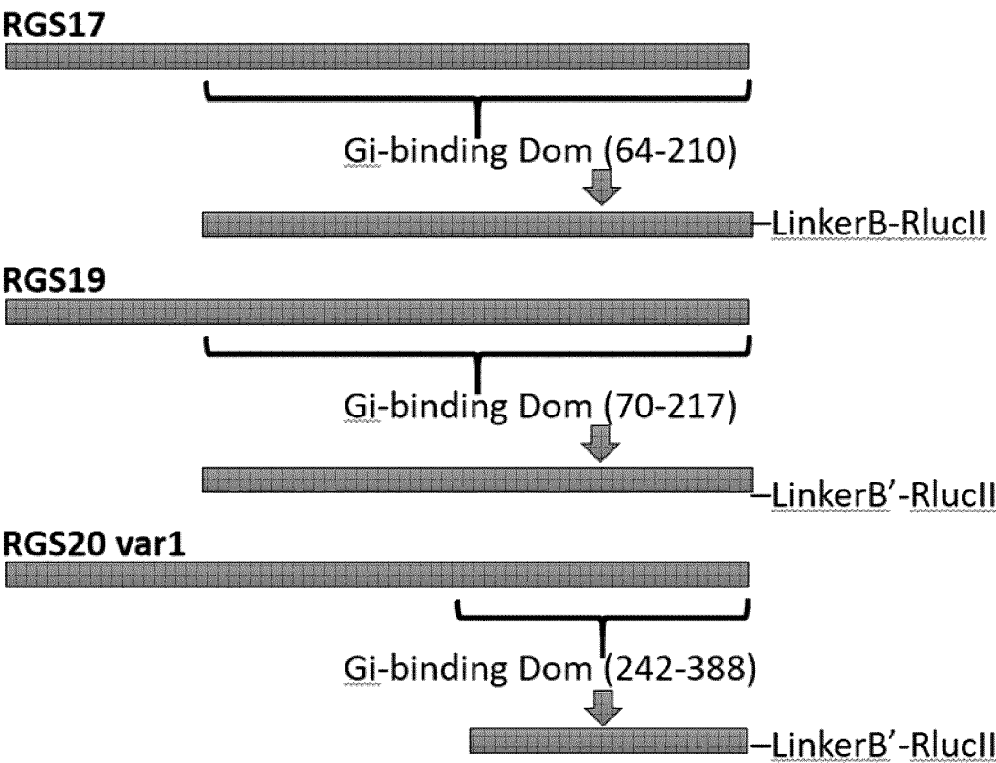


FIG. 2Z



LinkerB'=GSAGTGGRAIDIKLASAT

FIG. 3A

DRC: Dopamine/D4R, RGS17-based sensor

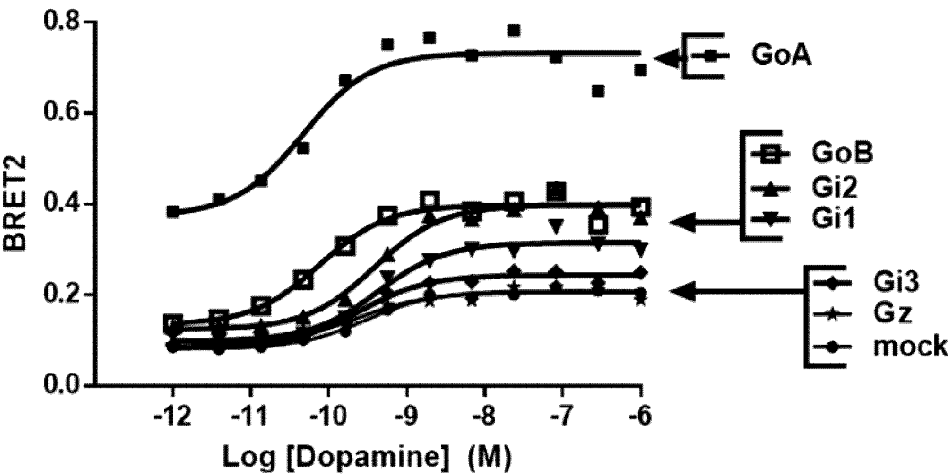


FIG. 3B

DRC: Dopamine/D4R, RGS19-based sensor

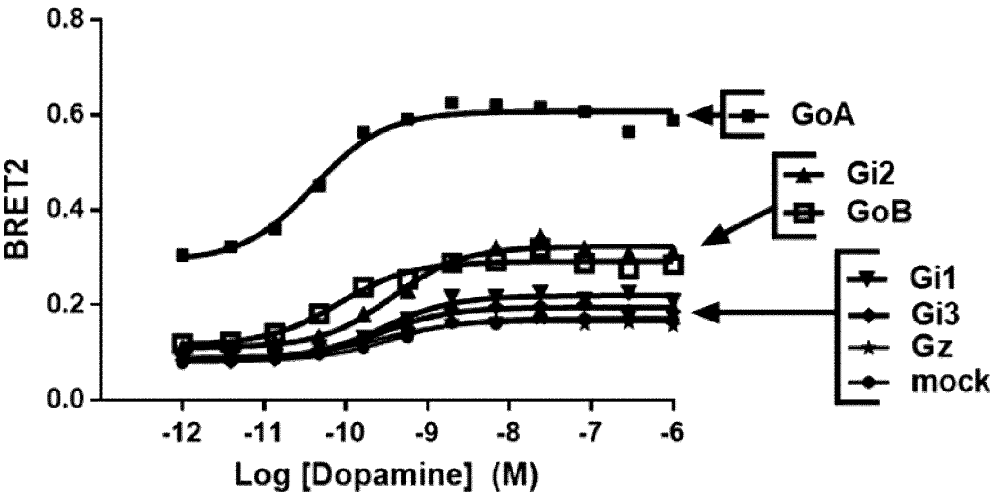


FIG. 3C

DRC: Dopamine/D4R, RGS20-based sensor

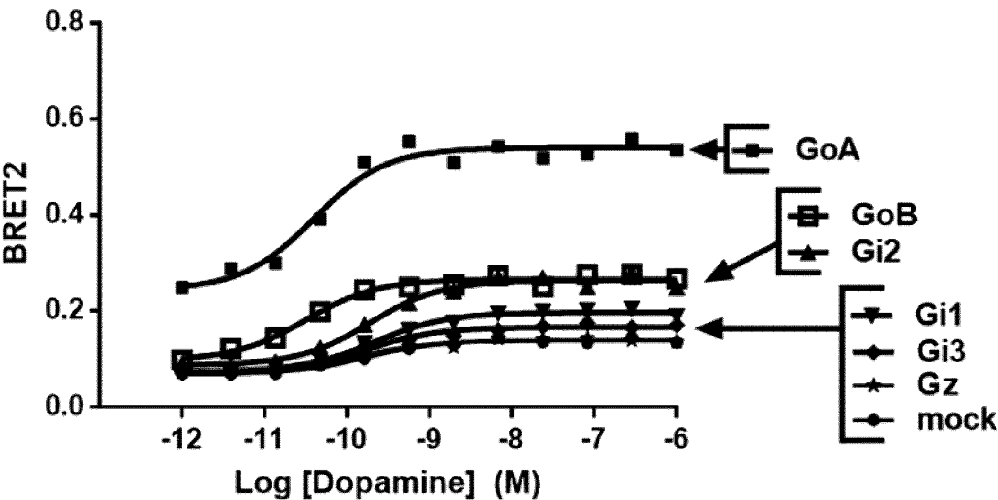
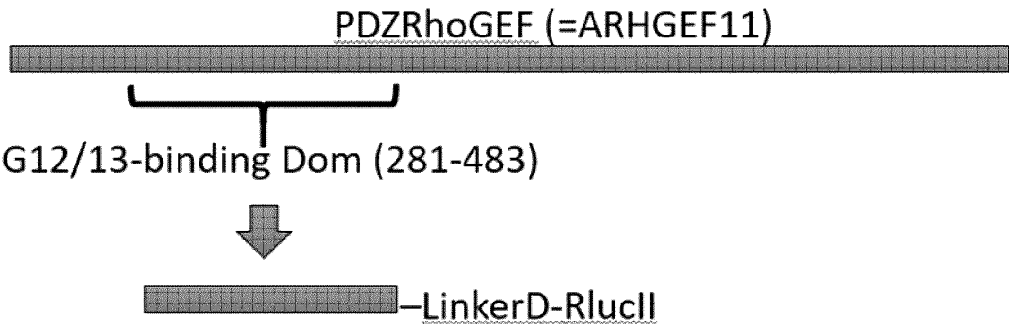


FIG. 3D



RlucII-tagged cytosolic G12/13 interacting domain of PDZ Rho GEF

LinkerD= GIRLREALKLPAT

FIG. 4A

DRC TPαR/I-BOP, PDZRG-RlucII vs G12/rGFP-CAAX

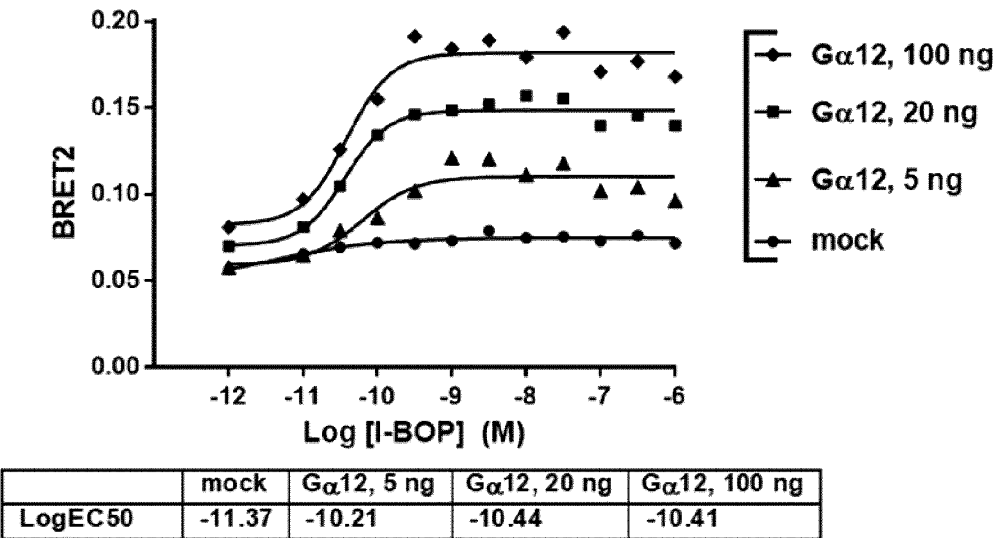


FIG. 4B

DRC TP α R/I-BOP, PDZRG-RlucII vs G13/rGFP-CAAX

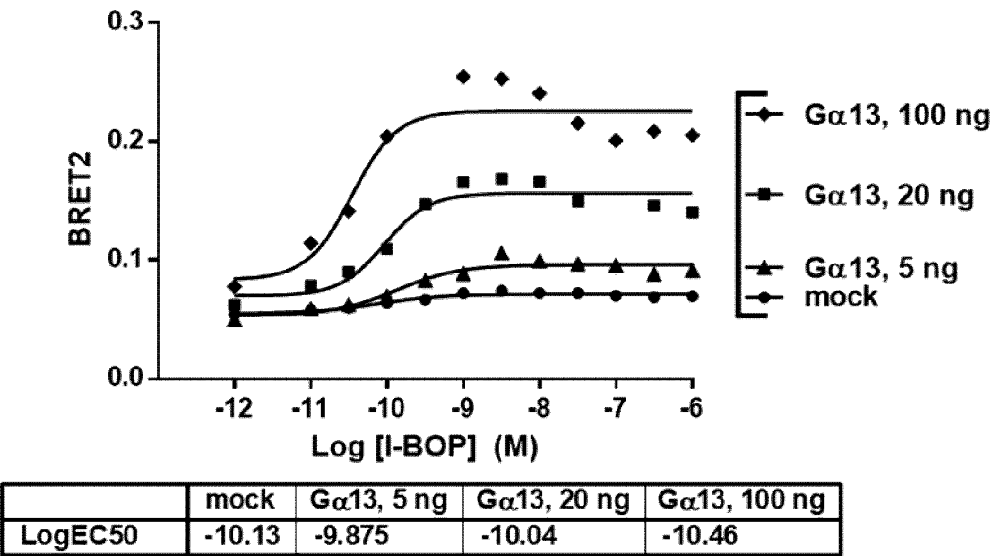


FIG. 4C

DRC TP α R, PDZRG-RlucII vs G12/rGFP-CAAX

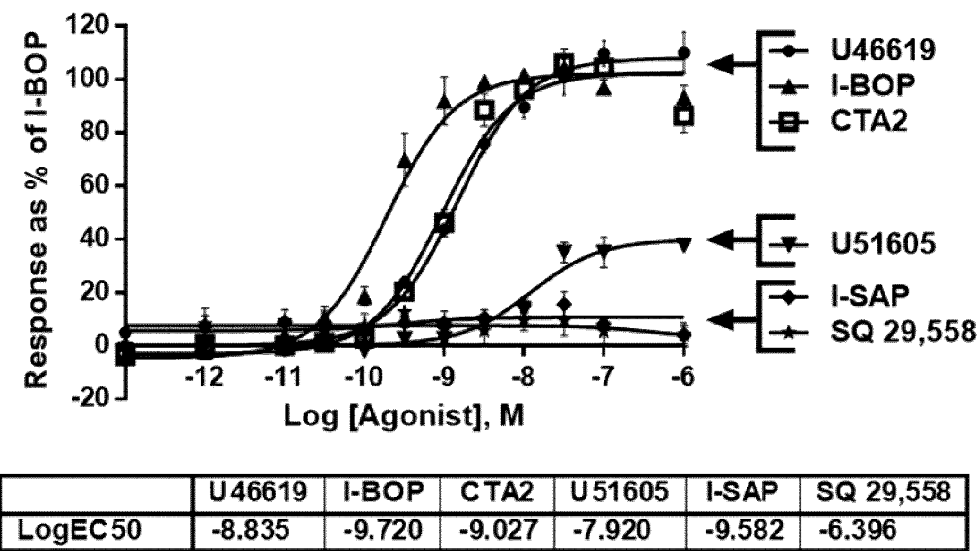
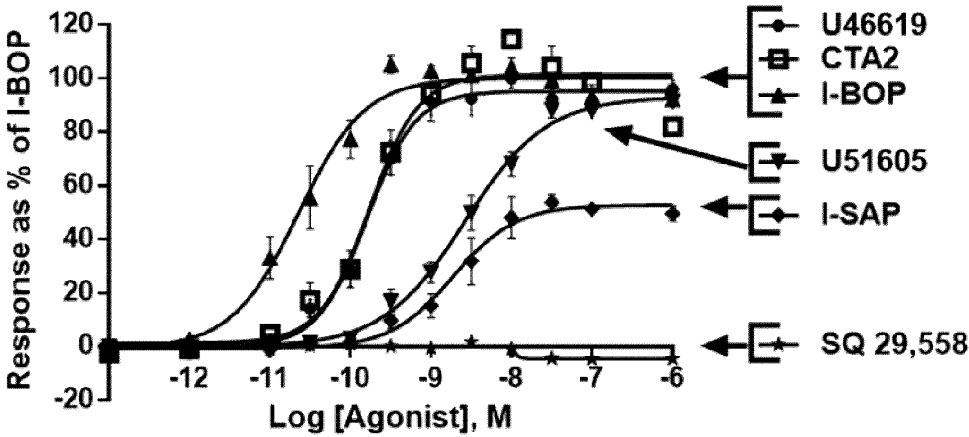


FIG. 4D

DRC TP α R, PDZRG-RlucII vs G13/rGFP-CAAX



	U46619	I-BOP	CTA2	U51605	I-SAP	SQ 29,558
LogEC50	-9.796	-10.65	-9.765	-8.583	-8.727	~ -7.959

FIG. 4E

Z'Factor:TP α R, pDZRG-RlucII/G12 sensor

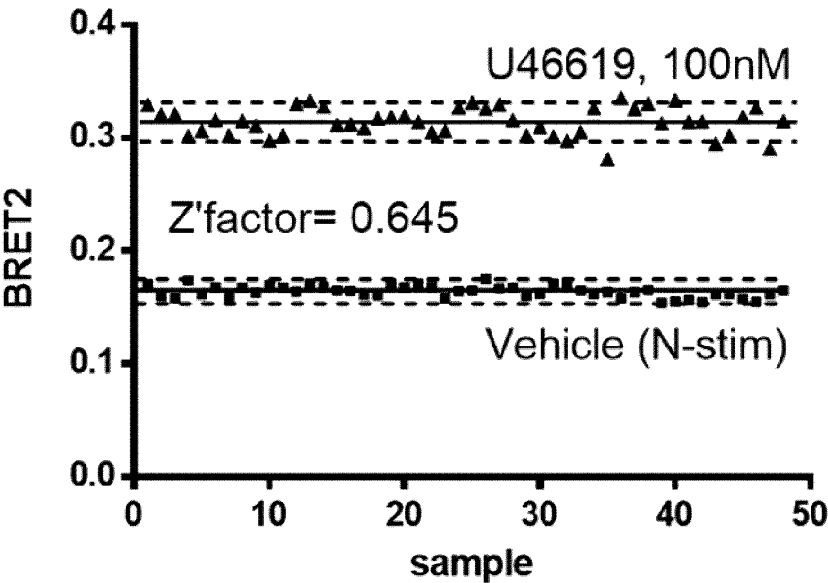
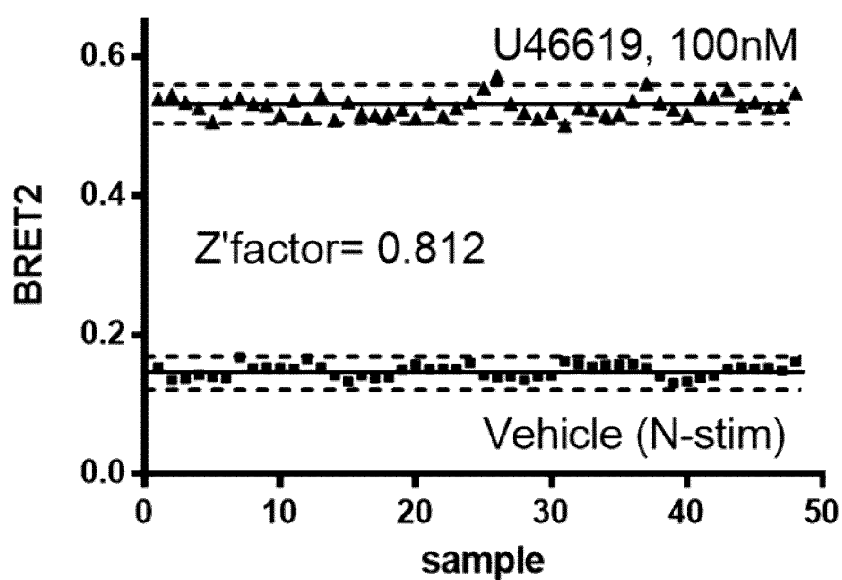
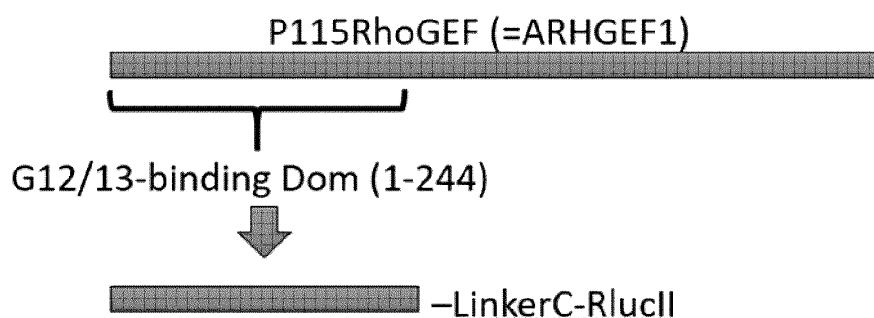


FIG. 4F

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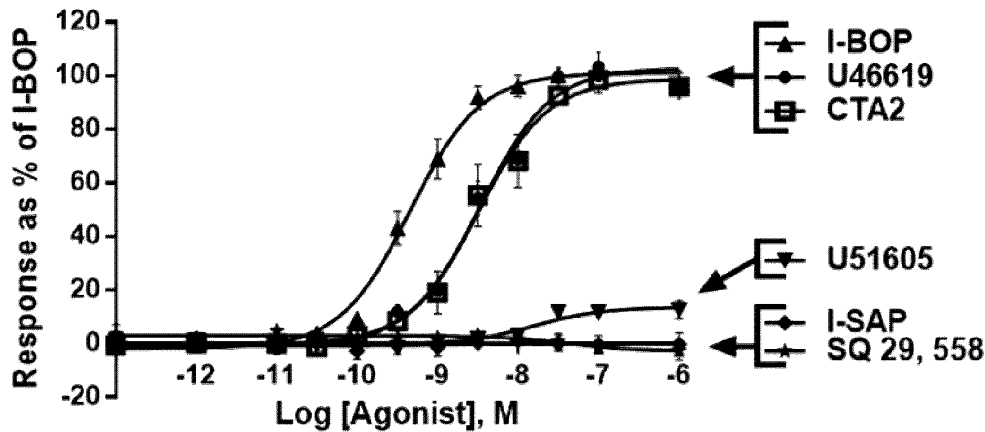
Z'Factor: TP α R, PDZRG-RlucII/G13 sensor**FIG. 4G**

RlucII-tagged cytosolic G12/13 interacting domain of P115 Rho GEF

LinkerC= RLKLPAT

FIG. 5A

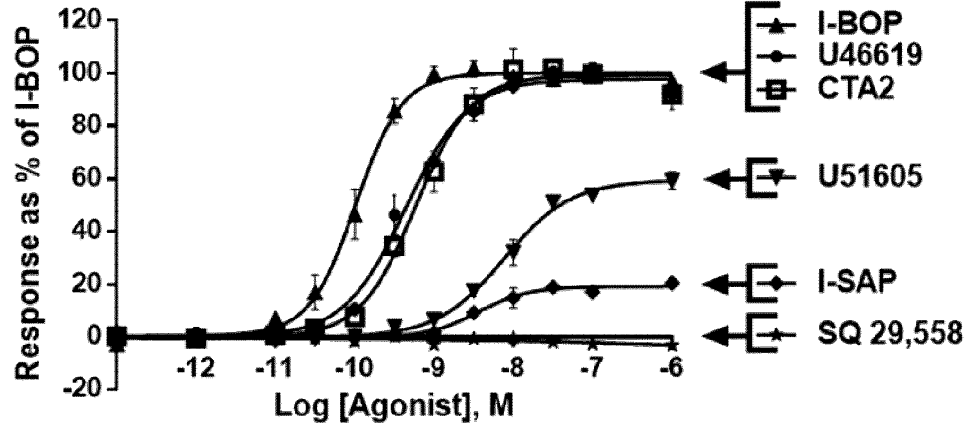
DRC TP α R, P115RG-RlucII vs G12/rGFP-CAAX



	U46619	I-BOP	CTA2	U51605	I-SAP	SQ 29, 558
LogEC50	-8.470	-9.341	-8.499	-7.804	-8.620	-7.373

FIG. 5B

DRC TP α R, P115RG-RlucII vs G13/rGFP-CAAX



	U46619	I-BOP	CTA2	U51605	I-SAP	SQ 29,558
LogEC50	-9.356	-9.986	-9.232	-8.119	-8.444	17.94

FIG. 5C

Z'Factor:TP α R, p115RG-RlucII/G12 sensor

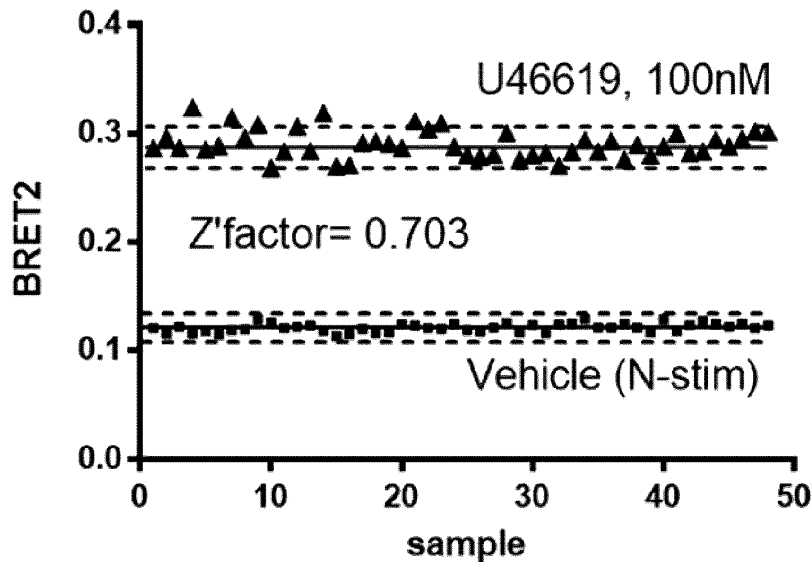


FIG. 5D

Z'Factor:TP α R, p115RG-RlucII/G13 sensor

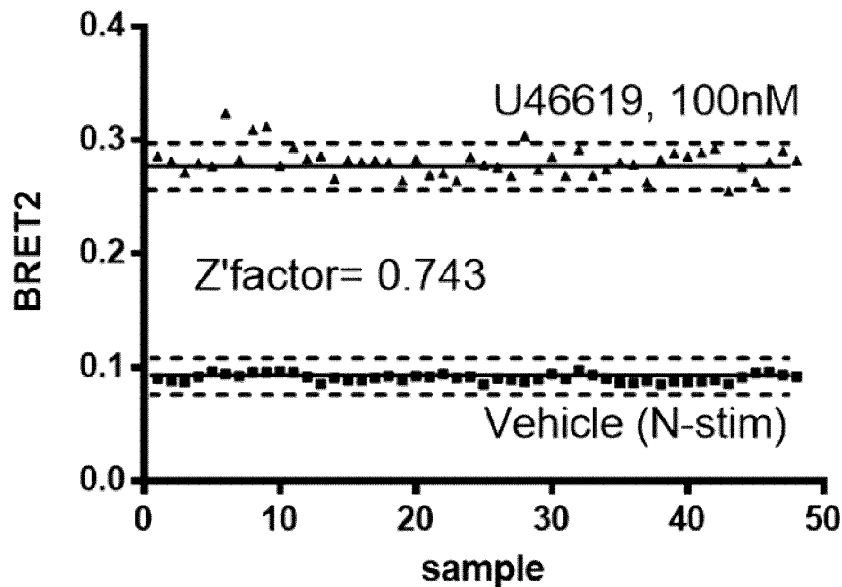
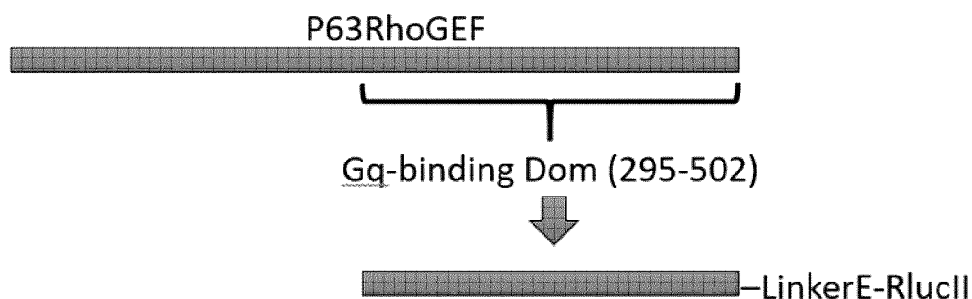


FIG. 5E

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RlucII-tagged cytosolic fragment of p63 (lacking the membrane tethering portion of the protein) containing only the Gq binding domain

LinkerE=ASGSAGTGGRAIDIKLPAT

FIG. 6A

DRC TP α R/U46619, p63RG-RlucII/Gq vs PM

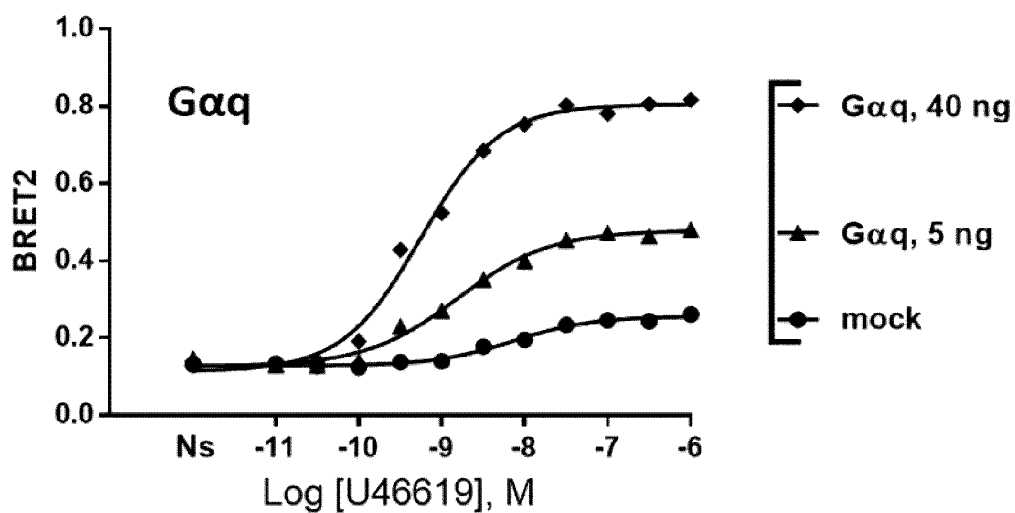


FIG. 6B

DRC:TP α R/U46619, p63RG-RlucII/G11 vs PM

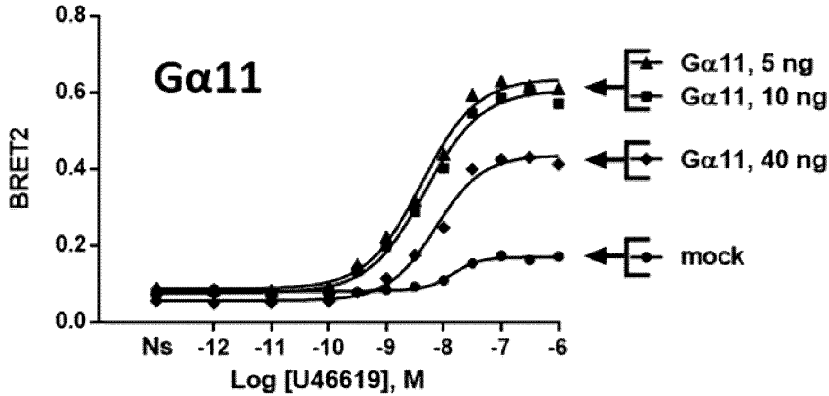


FIG. 6C

DRC:TP α R/U46619, p63RG-RlucII/G14 vs PM

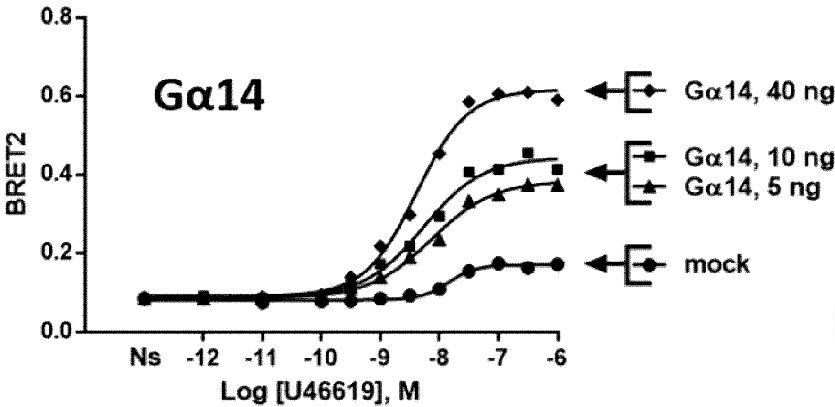


FIG. 6D

DRC:TP α R/U46619, p63RG-RlucII/G15 vs PM

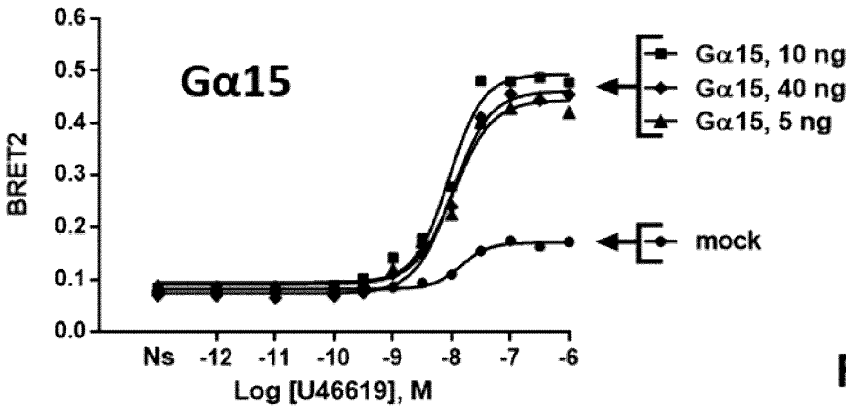


FIG. 6E

DRC: TP α R/U46619, p63RG-RlucII/Gq vs EE

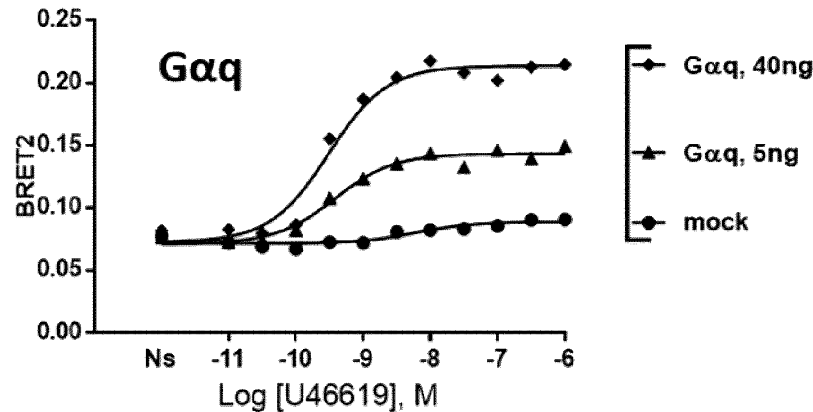


FIG. 6F

DRC: TP α R/U46619, p63RG-RlucII/G11 vs EE

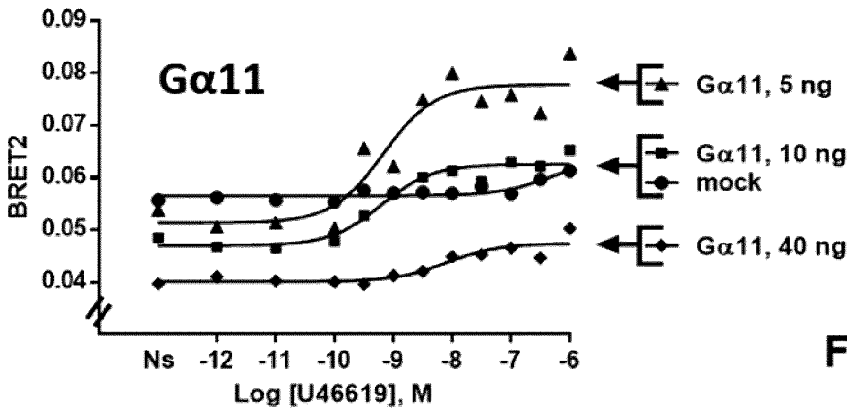


FIG. 6G

DRC: TP α R/U46619, p63RG-RlucII/G14 vs EE

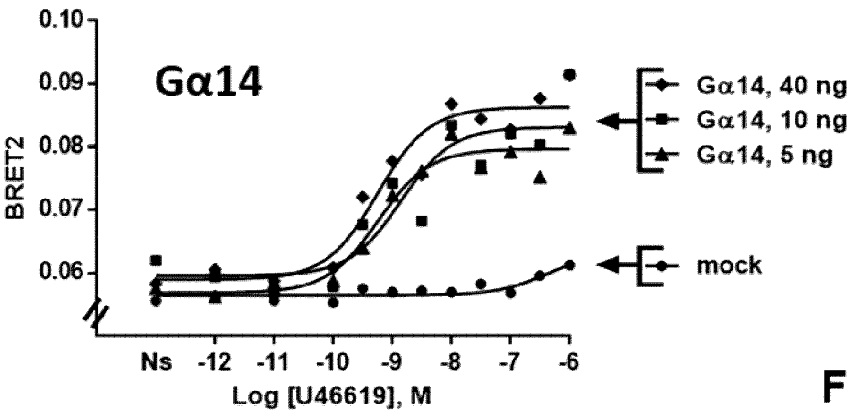


FIG. 6H

DRC:TPαR/U46619, p63RG-RlucII/G15 vs EE

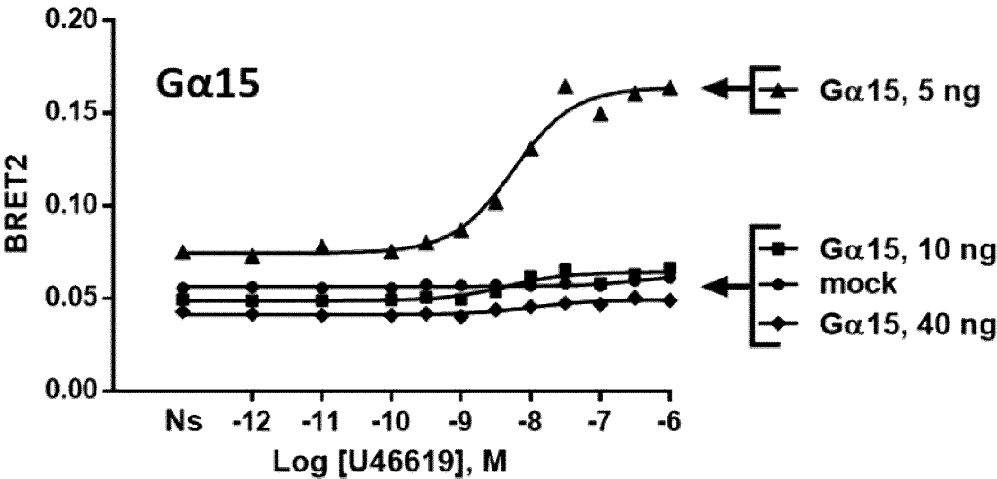
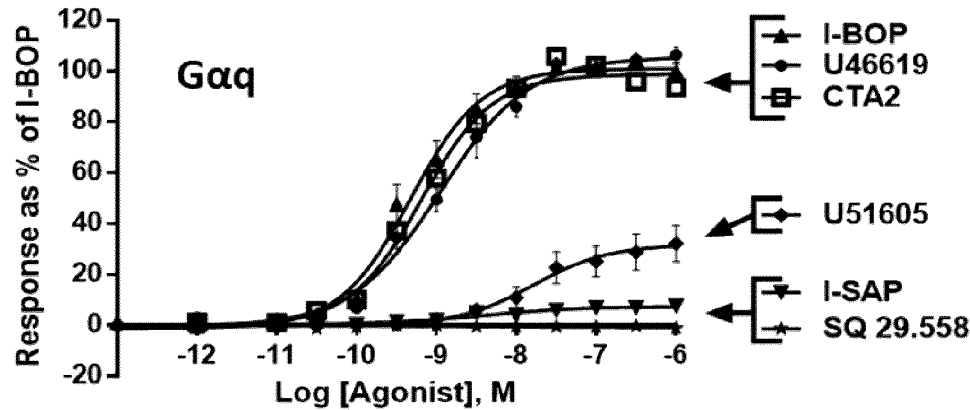


FIG. 6I

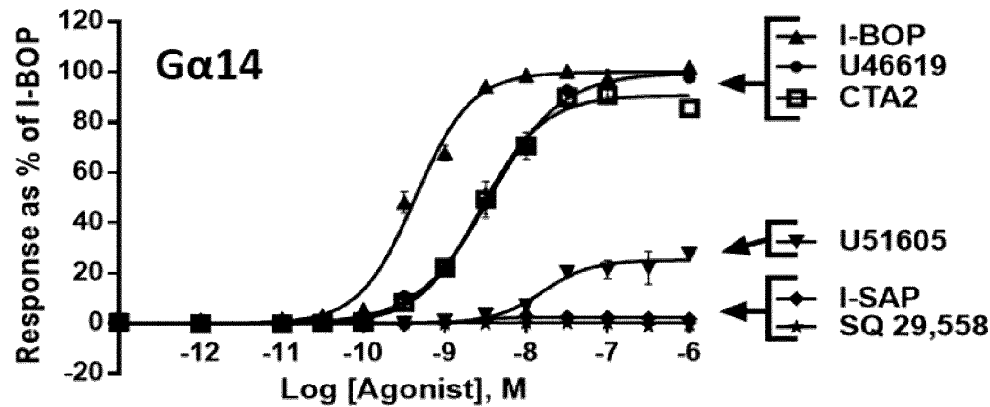
DRC TPαR, p63-RlucII vs Gαq/rGFP-CAAX



	U46619	I-BOP	I-SAP	CTA2	U51605	SQ 29.558
LogEC50	-8.955	-9.324	-8.404	-9.192	-7.787	-94.50

FIG. 6J

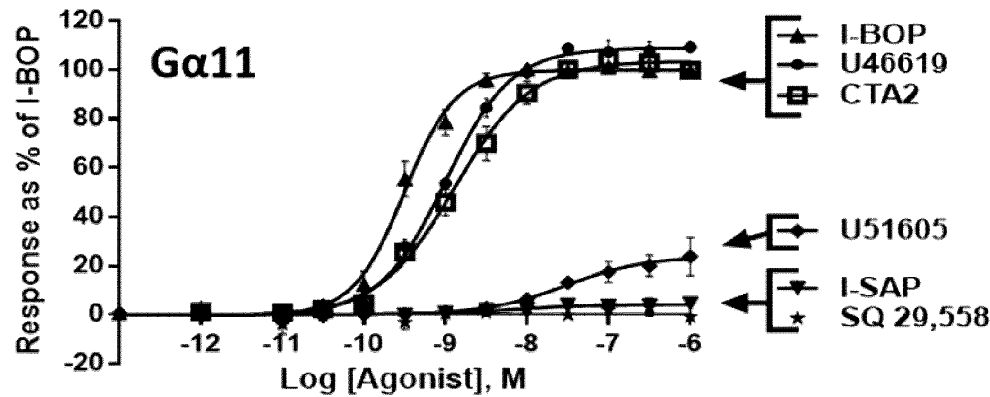
DRC TP α R, p63-RlucII vs G α 14/rGFP-CAAX



	U46619	I-BOP	CTA2	U51605	I-SAP	SQ 29,558
LogEC50	-8.457	-9.362	-8.563	-7.798	-8.579	

FIG. 6K

DRC TP α R, p63-RlucII vs G α 11/rGFP-CAAX

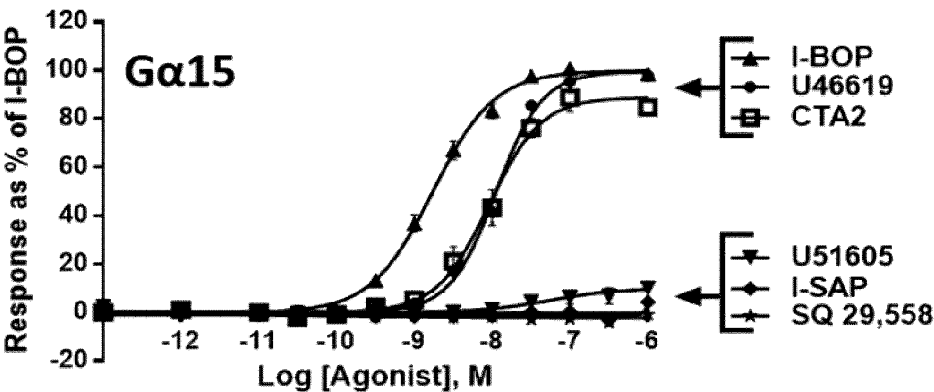


	U46619	I-BOP	I-SAP	CTA2	U51605	SQ 29,558
LogEC50	-9.001	-9.506	-8.220	-8.894	-7.513	

FIG. 6L

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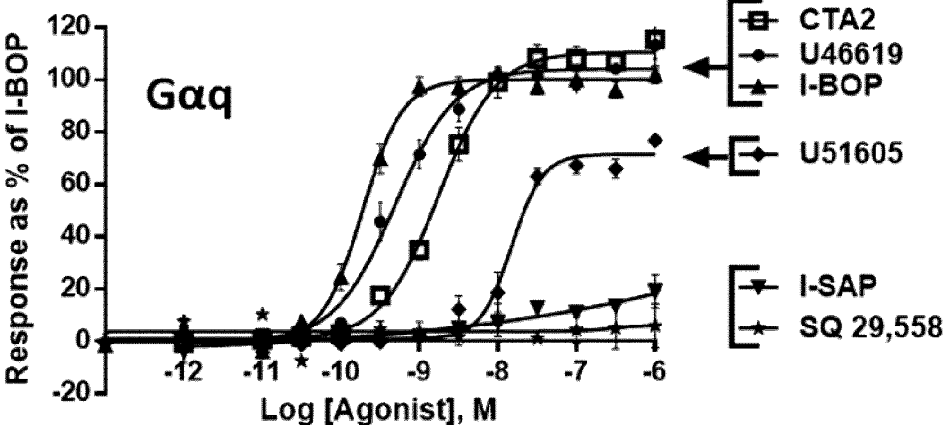
DRC TPαR, p63-RlucII vs Gα15/rGFP-CAAX



	U46619	I-BOP	CTA2	U51605	I-SAP	SQ 29,558
LogEC50	-7.952	-8.766	-8.041	-7.257	~ -5.983	-10.89

FIG. 6M

DRC TPαR, p63-RlucII vs Gαq/rGFP-FYVE



	U46619	I-BOP	I-SAP	CTA2	U51605	SQ 29,558
LogEC50	-9.313	-9.723	~ 3.747	-8.759	-7.827	-6.554

FIG. 6N

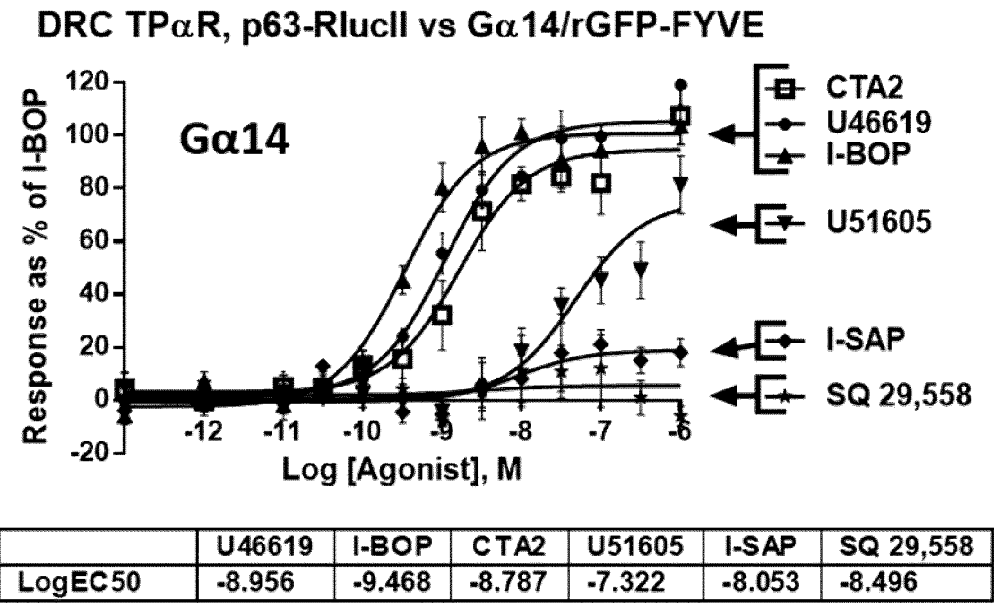


FIG. 6O

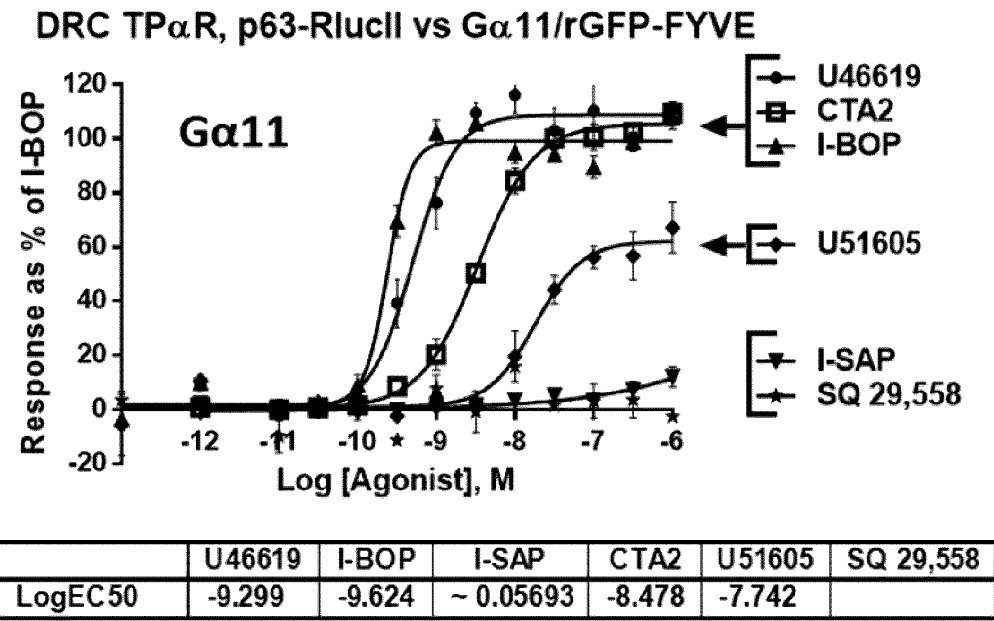
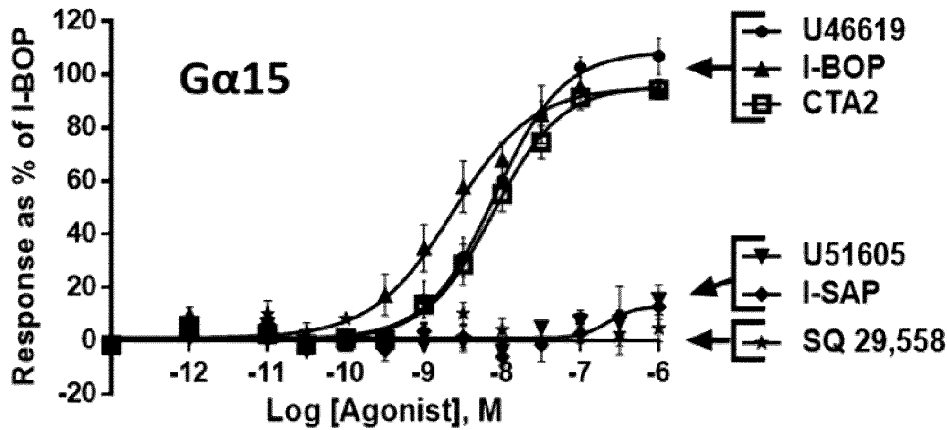


FIG. 6P

DRC TP α R, p63-RlucII vs G α 15/rGFP-FYVE



	U46619	I-BOP	CTA2	U51605	I-SAP	SQ 29,558
LogEC50	-8.089	-8.633	-8.115		-6.644	

FIG. 6Q

Z'Factor:TP α R, p63RG-RlucII/Gq sensor

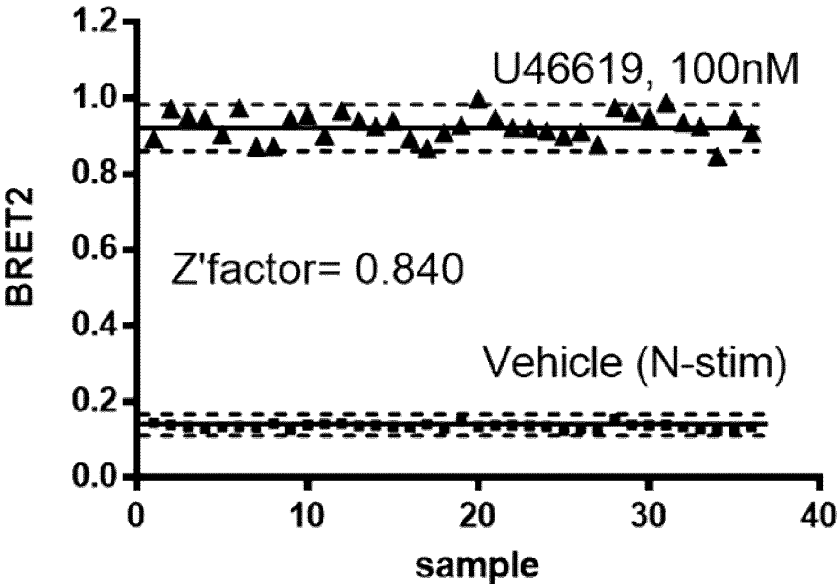


FIG. 6R

Z'Factor: TP α R, p63RG-RlucII/Gq sensor

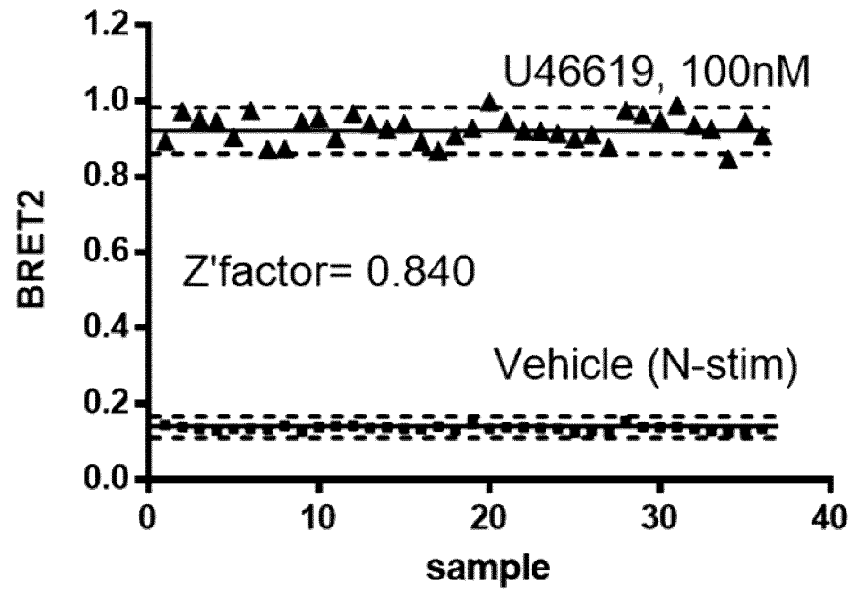
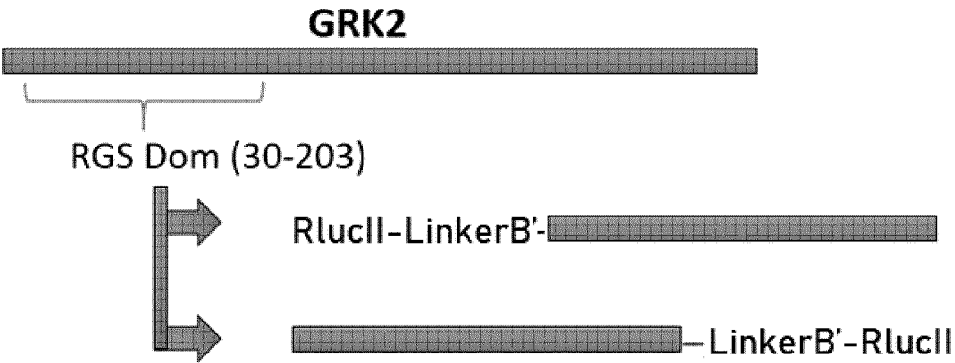


FIG. 6S

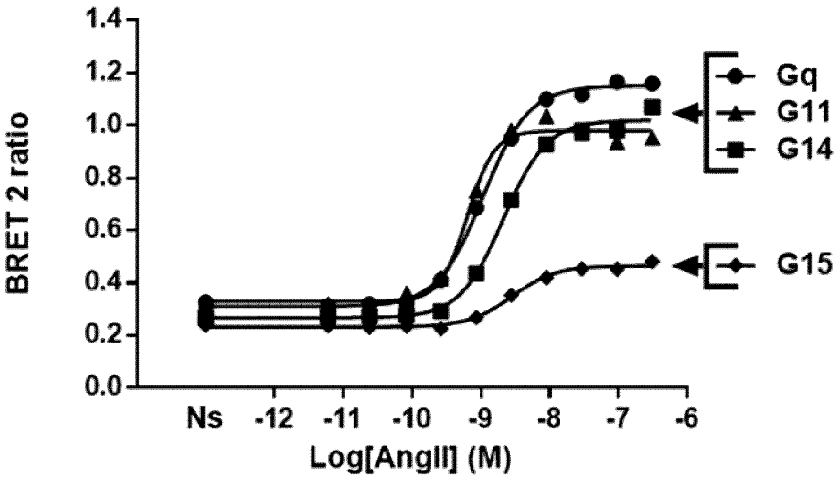


RlucII-tagged cytosolic Gq interacting RGS domain of GRK2

LinkerB' =GSAGTGGRAIDIKLASAT

FIG. 7A

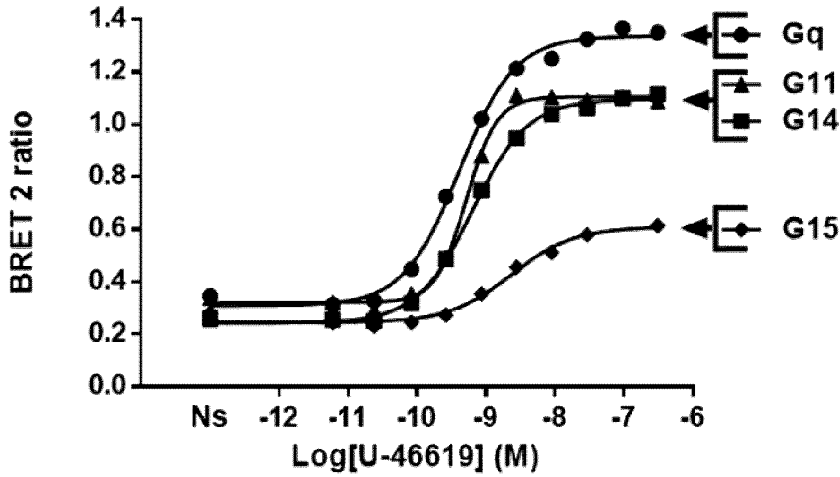
DRC AT1aR/AngII: RIucII-RGS(GRK2) vs Gα/rGFP-CAAX



	Gq	G11	G14	G15
LogEC50	-8.965	-9.196	-8.674	-8.546

FIG. 7B

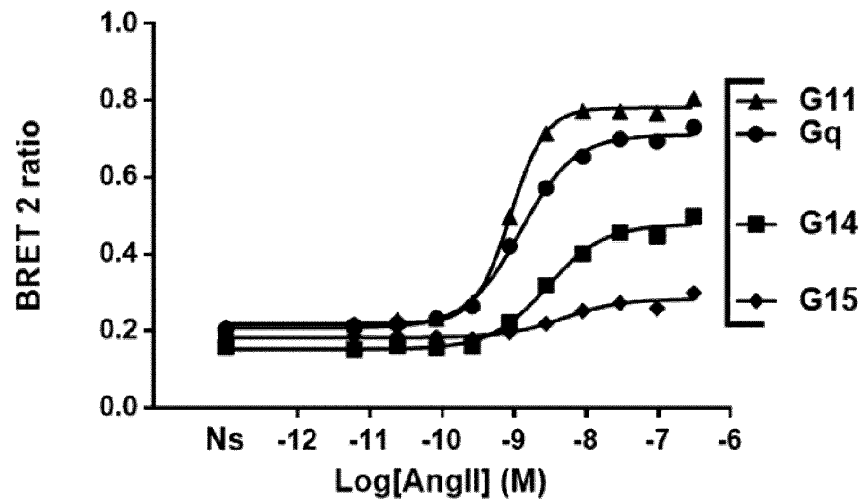
DRC TPαR/U46619: RIucII-RGS(GRK2) vs Gα/rGFP-CAAX



	Gq	G11	G14	G15
LogEC50	-9.387	-9.284	-9.198	-8.631

FIG. 7C

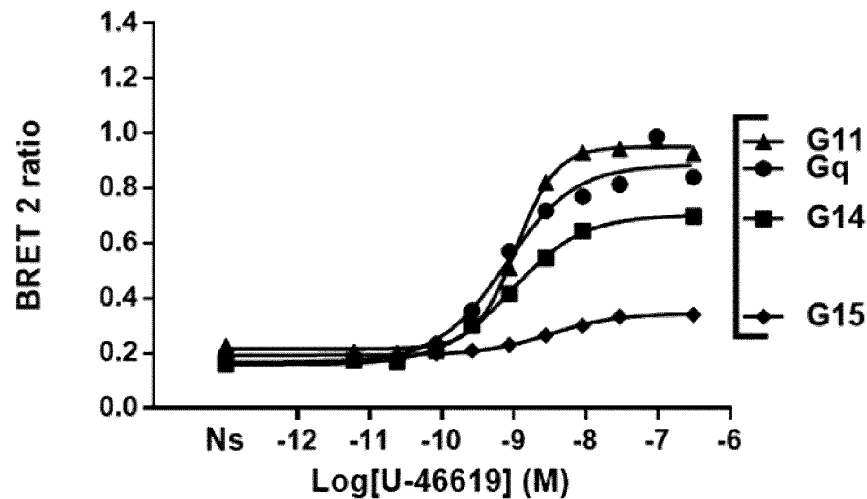
DRC AT1aR/AngII: RGS(GRK2)-RlucII vs Gα/rGFP-CAAX



	Gq	G11	G14	G15
LogEC50	-8.914	-9.055	-8.543	-8.324

FIG. 7D

DRC TPαR/U46619: RGS(GRK2)-RlucII vs Gα/rGFP-CAAX



	Gq	G11	G14	G15
LogEC50	-9.107	-8.969	-9.024	-8.514

FIG. 7E

Z'Factor:TP α R, RlucII-RGS(GRK2)/Gq sensor

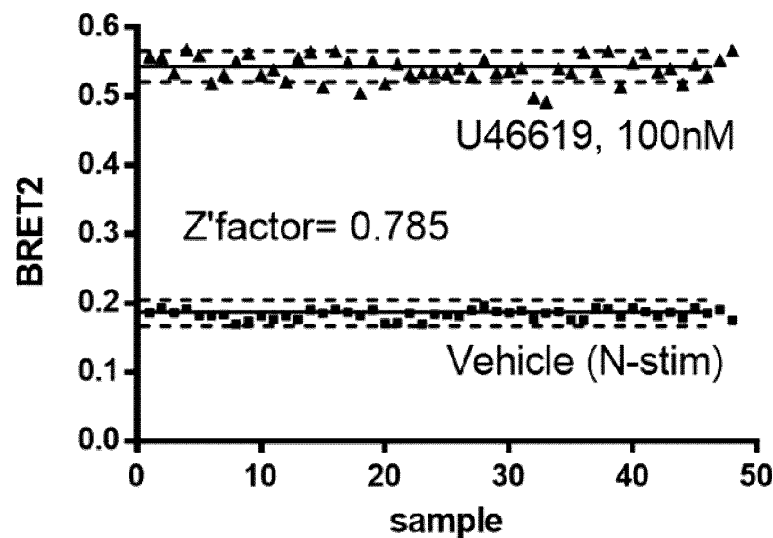
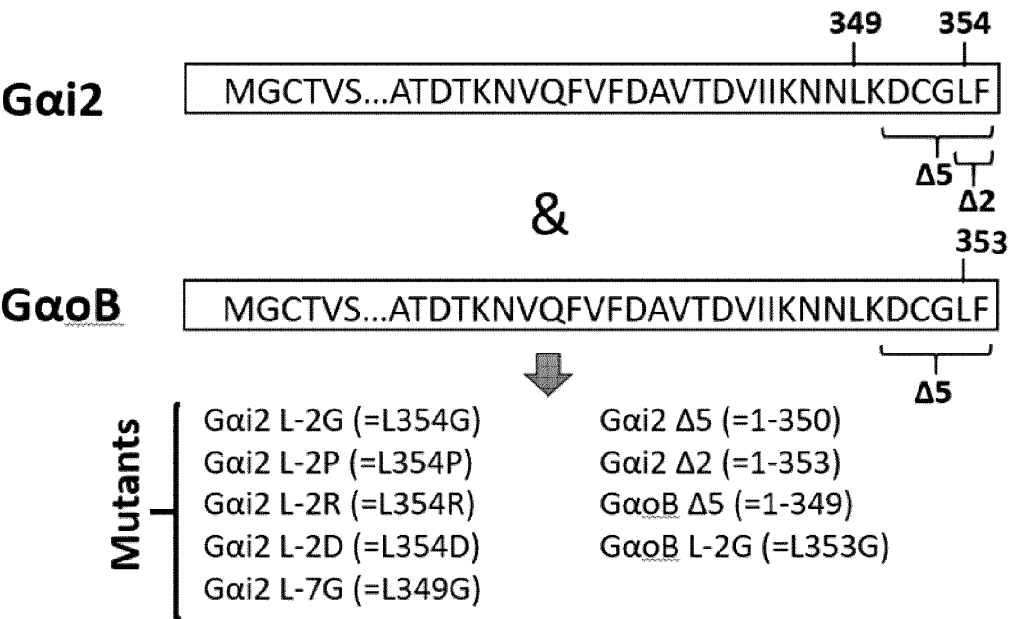


FIG. 7F



Mutations that prevent GPCR-mediated Gprotein activation,
while keeping GIV/Girdin-mediated Gprotein activation

FIG. 8A

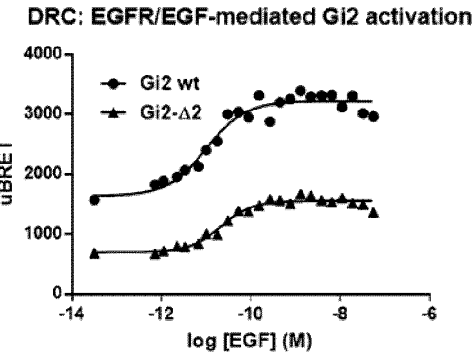


FIG. 8B

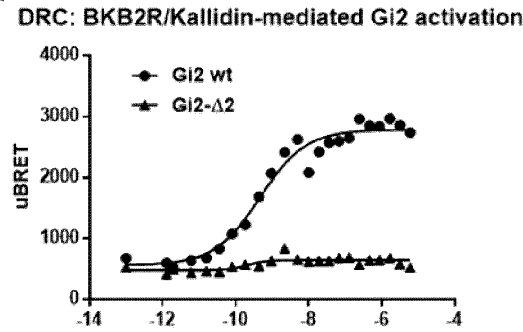


FIG. 8C

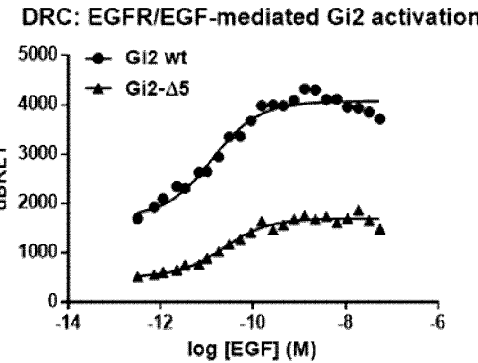


FIG. 8D

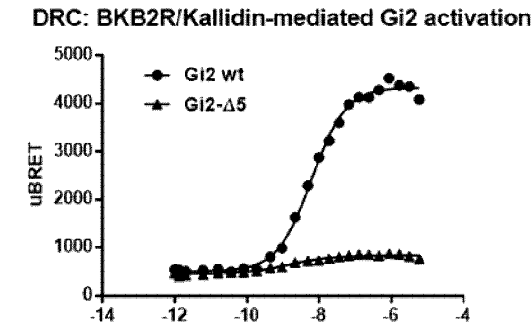


FIG. 8E

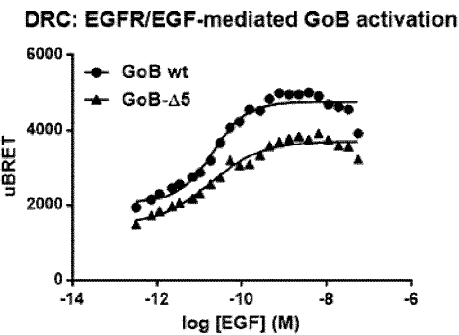


FIG. 8F

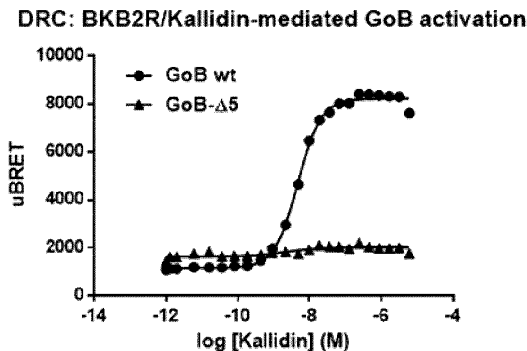


FIG. 8G

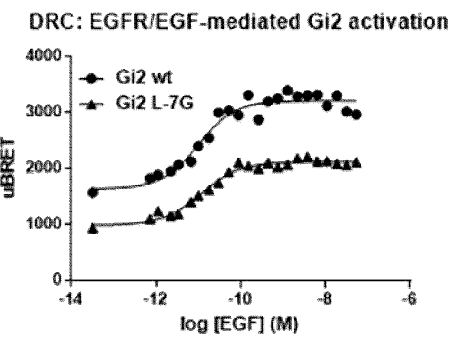


FIG. 8H

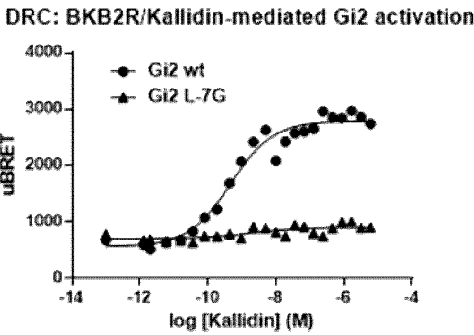


FIG. 8I

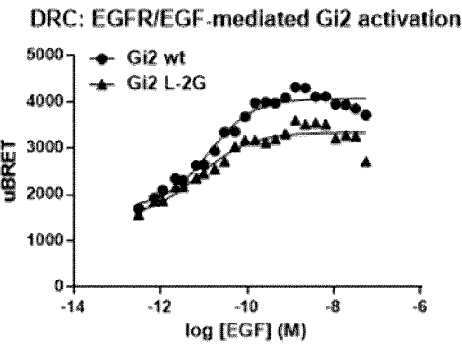


FIG. 8J

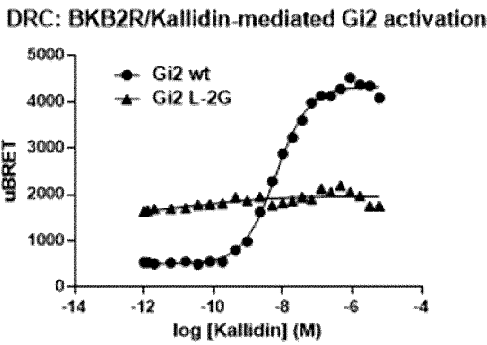


FIG. 8K

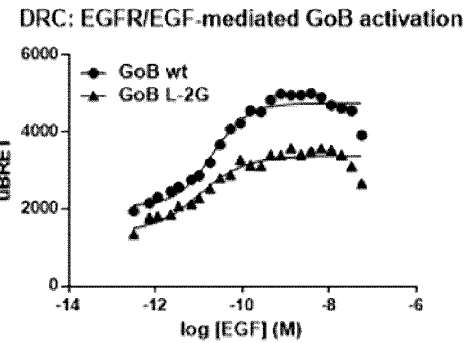


FIG. 8L

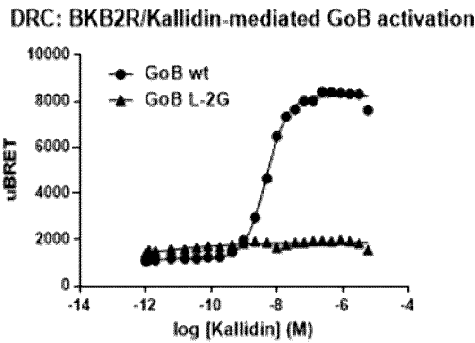


FIG. 8M

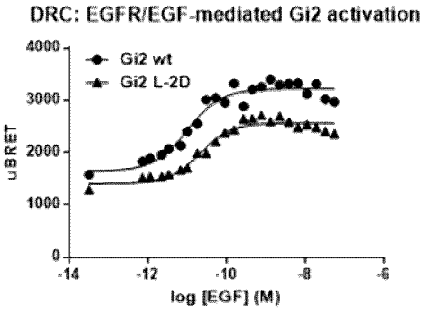


FIG. 8N

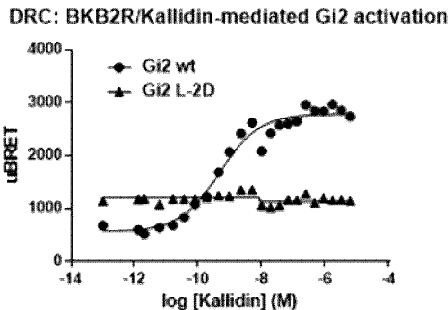


FIG. 8O

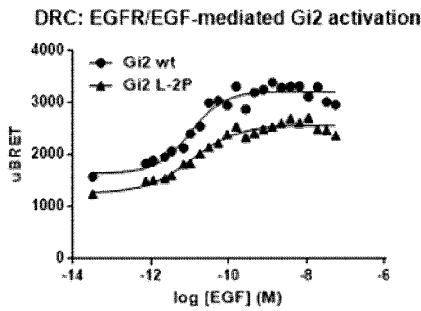


FIG. 8P

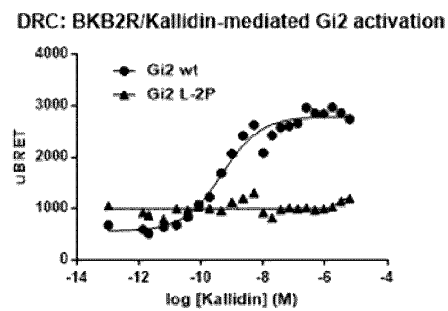


FIG. 8Q

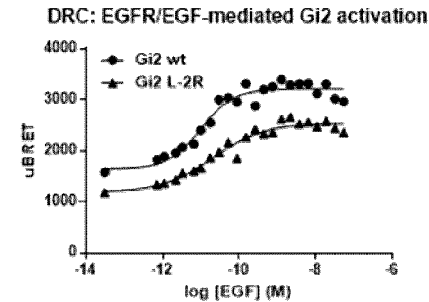


FIG. 8R

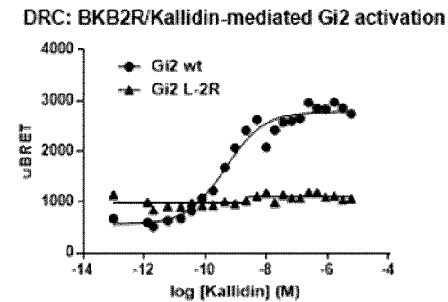


FIG. 8S

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Z' factor: EGFR, Rap1GAP (SSS-AAA)/Gi2-WT

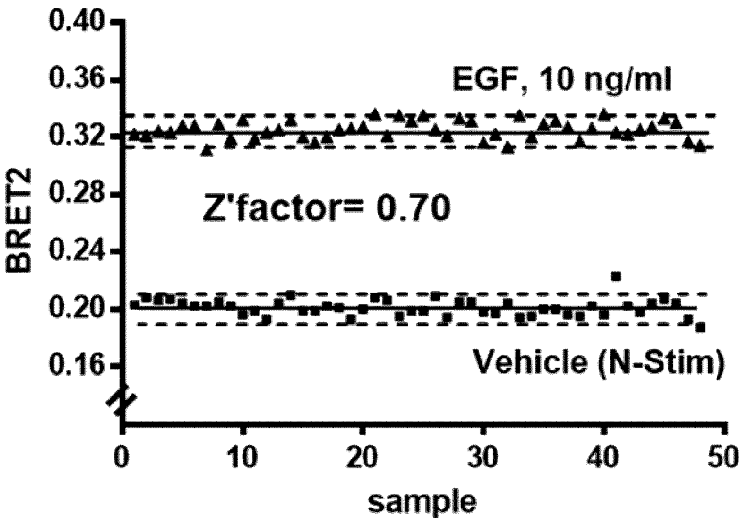


FIG. 8T

Z' factor: EGFR, Rap1GAP (SSS-AAA)/Gi2_L-2P

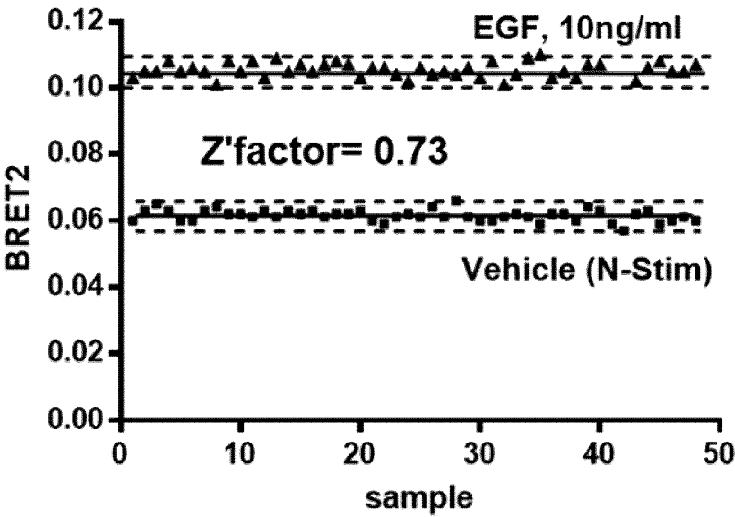


FIG. 8U

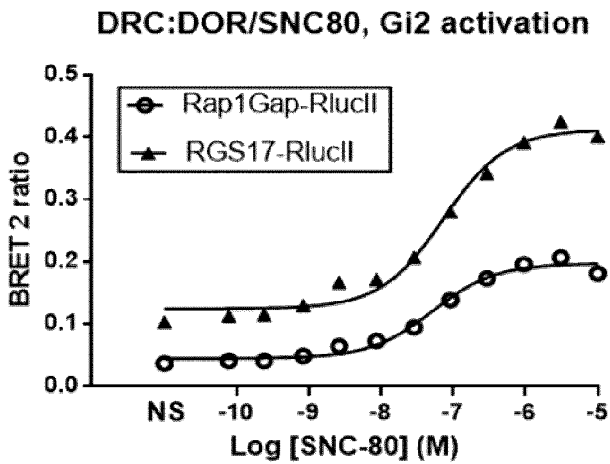


FIG. 8V

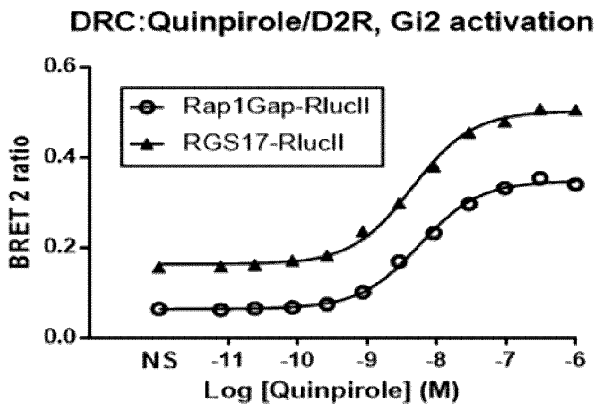


FIG. 8W

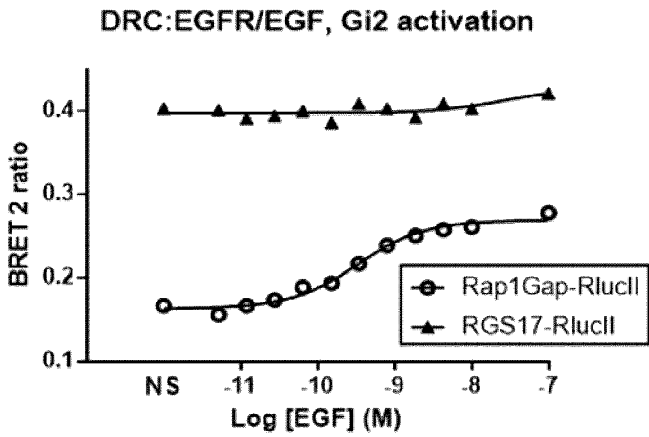


FIG. 8X

>Rap1GAP (1-442) (SEQ ID NO: 8)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKMEENGSGGGGFESFKRVIRSRSQSM

>Rap1GAP ΔSSS (1-436) (SEQ ID NO: 9)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKMEENGSGGGGFESFKRVIR

>Rap1GAP (1-420) (SEQ ID NO: 10)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKME

>Rap1GAP SSS-AAA (1-442; S437A/S439A/S441A) (SEQ ID NO: 11)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKMEENGSGGGGFESFKRVIRARAQAM

>Rap1GAP SSS-TTT (1-442; S437T/S439T/S441T) (SEQ ID NO: 12)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKMEENGSGGGGFESFKRVIRTRTQTM

>Rap1GAP SS-AA (1-442; S437A/S441A) (SEQ ID NO: 13)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKMEENGSGGGGFESFKRVIRARSQAM

>Rap1GAP SS-DA (1-442; S437A/S441A) (SEQ ID NO: 14)
MIEKMQGSRMDEQRCSFPPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLQSPTTKVK
LECNPTARIYRKHFLGKEHFNYYSLDAALGHLVFSKYDVIQDQHLRLLLRKCRITYHDVIPISCLTEFPNVVQMAKL
CEDVNVDREFYPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLGQTSEEEELFSTNEESPAFVEFLEFLGQKVKLQDFKGR
GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQQRKHIGAAIVAVVFQDENTPFVPDMIASNFLHAYVVV
QAEGGGPDGPLYKVSVTARDDVPFFGPPPLDPAVFRKGPEFQEFLLTKLINAEYACYKAEKFAKLEERTRAALLETL YEE
LHIHSQSMMLGGDEDEKMEENGSGGGGFESFKRVIRDRSQAM

FIG. 9A

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>Rap1GAP SS-AD (1-442; S437A/S441D) (SEQ ID NO: 15)
 MIEKMQGSRMDEQRCSEFPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLOSPPTTKVK
 LECNPTARIYRKHFLGKEHFNYSLDAALGHLVFSKYDVIQDQEHRLRLRLTKCRTYHDVIPISCLTEFPNVVQMAKL
 CEDVNVDRFPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLQGTSEELFSTNEESPAFVEFLEFLGQKVKLQDFKGF
 GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQKRKHIGAAIVAVVFQDENTPFVPMIASNFLHAYVVV
 QAEGGGPDGPLYKVSVTARDDVPFFGPPLEDDPAVFRKGPEFQEFLLTKLINA EYACYKAEKFAKLEERTRAALETLYEE
 LHIHSQSMMLGGDEDKMENSGGGGFESFKRVIRARSQDM

>Rap1GAP SS-DD (1-442; S437A/S441A) (SEQ ID NO: 16)
 MIEKMQGSRMDEQRCSEFPPLKTEEDYIPYPSVHEVLGREGPFPLILLPQFGGYWIEGTNHEITSIPETEPLOSPPTTKVK
 LECNPTARIYRKHFLGKEHFNYSLDAALGHLVFSKYDVIQDQEHRLRLRLTKCRTYHDVIPISCLTEFPNVVQMAKL
 CEDVNVDRFPVLYPKASRLIVTFDEHVISNNFKFGVIYQKLQGTSEELFSTNEESPAFVEFLEFLGQKVKLQDFKGF
 GGLDVTHGQTGTESVYCNFRNKEIMFHVSTKLPYTEGDAQQLQKRKHIGAAIVAVVFQDENTPFVPMIASNFLHAYVVV
 QAEGGGPDGPLYKVSVTARDDVPFFGPPLEDDPAVFRKGPEFQEFLLTKLINA EYACYKAEKFAKLEERTRAALETLYEE
 LHIHSQSMMLGGDEDKMENSGGGGFESFKRVIRDRSQDM

>P63 RGS (residues 295-502 of SEQ ID NO: 25)
 MIMKYQLLLKDFLKYYNRAGMDTADLEQAVEVMCFVPKRCNDMMTLGRLRGFEGKLTAGQKLLGQDTFWVTEPEAGLLS
 SGRERRRVFLFEQIIIFSEALGGVVRGGTQPGYVYKNSIKVSCLGLEGNLQGDPCRFAITSRGPEGGIQRVVLQAADPAI
 SQAWIKHVAQILESQRDFLNLQSPIEQRRRESQTNSLGRPRGPGVGSP

>PDZRG (=ARHGEF11) (residues 281-483 of SEQ ID NO: 21)
 QGVDSQSPKPLIIGPEEDYDPGYFNNESEDIIQDLEKLKSRPAHLGVFLRYIFSQADPSPLLFYLCAEVYQQASPKDSRSL
 GKDIWNIFLEKNAPLRVKIPEMLQAEIDSRLNSEDARGVLCBAQEAAPEIQEQIHDYRTRKRTLGLSLYGENDLLDL
 GDPLRERQVAEKQLAALGDILSKYEEDRSAPMDFALNTYMSHA

>P115RG (=ARHGEF1, isoform var2) (residues 1-244 of SEQ ID NO:23)
 MEDFARGAASPGPSRPGVLVPVSIIGAEDDFENELETNSEEQNSQFQSLEQVKRRPAHLMALLQHVALQFEPGPLLCCCLH
 ADMLGSLGPKEAKKAFDFYHSEFLEKTAVLRVPVPPNVAFELDRTRADLISEDVQRRFVQEVVQSQQVAVGRQLEDFRSK
 RLGMGTPEWEQELAQLEAWVGRDRASYEARERHVAERLLMHLEEMQHTISTDEEKSAVVNIAIGLYMRHLGVRTKSGDKKS
 GRNF

>GRK2 RGS dom (residues 30-203 of SEQ ID NO: 27)
 KILLPEPSIRSVMQKYLEDRGEVTFEKIFSQKLGYLFRDFCLNLHLEEARPLVEFYEIKKYEKLETEEERVARSRIFD
 SYMKELLACSHPFKSKATEHVQGHGKKGVPDPDFQPIIEICQNLRGDVQKFIESDKFTRFCQWKNVLENIHLTMND
 FSVHRIIGRGFG

>Gα12 Δ5(=1-350) (SEQ ID NO: 28)
 MGCTVSAEDKAAERSKIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
 IMAIVKAMGNLQIDFADPSRADDARQLFALSCTAEEQVLPDDLSGVIRRLWADHGVQACFGRSREYQLNDSAAYYLNDL
 ERIAQSDYIPTQQDVLRTVKTGTGIVETHFTFKDLHFKMFDVGGQSRERKKWIHCFEGVTAIIFCVALSAYDLVLAEDDEE
 MNRMHESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKITHSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
 YTHFTCATDTKNVQFVDAVTDVVIKNNLK

>Gα12 Δ2(=1-353) (SEQ ID NO: 29)
 MGCTVSAEDKAAERSKIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
 IMAIVKAMGNLQIDFADPSRADDARQLFALSCTAEEQVLPDDLSGVIRRLWADHGVQACFGRSREYQLNDSAAYYLNDL
 ERIAQSDYIPTQQDVLRTVKTGTGIVETHFTFKDLHFKMFDVGGQSRERKKWIHCFEGVTAIIFCVALSAYDLVLAEDDEE
 MNRMHESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKITHSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
 YTHFTCATDTKNVQFVDAVTDVVIKNNLKDCG

>Gα12 L-7G(=L349G) (SEQ ID NO: 30)
 MGCTVSAEDKAAERSKIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
 IMAIVKAMGNLQIDFADPSRADDARQLFALSCTAEEQVLPDDLSGVIRRLWADHGVQACFGRSREYQLNDSAAYYLNDL
 ERIAQSDYIPTQQDVLRTVKTGTGIVETHFTFKDLHFKMFDVGGQSRERKKWIHCFEGVTAIIFCVALSAYDLVLAEDDEE
 MNRMHESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKITHSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
 YTHFTCATDTKNVQFVDAVTDVVIKNNLKDCGLF

FIG. 9B

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>Gαi2 L-2G(=L354G) (SEQ ID NO: 31)
MGCTVSAEDKAAAERSKMIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
IMAI VKAMGNLQIDFADPSRADDARQLFALSCTAEEQGVLPDDL SGVIRRLWADHGVQACFGRSREYQLNDSAAAYLNDL
ERIAQSDYIPTQQDVLRLTRVKTGTGIVETHFTFKDLHFKMFDVGGQRSEKRWIHC FEGVTAI IFCVALSAYDLVLAEDDEE
MNRMHESMKLFDSICNNKWFTDTSI ILFLNKKDLFEEKI THSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
YTHFTCATDTKNVQFVFDAVTDV I IKNNLKDCGGF

>Gαi2 L-2D(=L354D) (SEQ ID NO: 32)
MGCTVSAEDKAAAERSKMIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
IMAI VKAMGNLQIDFADPSRADDARQLFALSCTAEEQGVLPDDL SGVIRRLWADHGVQACFGRSREYQLNDSAAAYLNDL
ERIAQSDYIPTQQDVLRLTRVKTGTGIVETHFTFKDLHFKMFDVGGQRSEKRWIHC FEGVTAI IFCVALSAYDLVLAEDDEE
MNRMHESMKLFDSICNNKWFTDTSI ILFLNKKDLFEEKI THSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
YTHFTCATDTKNVQFVFDAVTDV I IKNNLKDCGDF

>Gαi2 L-2P(=L354P) (SEQ ID NO: 33)
MGCTVSAEDKAAAERSKMIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
IMAI VKAMGNLQIDFADPSRADDARQLFALSCTAEEQGVLPDDL SGVIRRLWADHGVQACFGRSREYQLNDSAAAYLNDL
ERIAQSDYIPTQQDVLRLTRVKTGTGIVETHFTFKDLHFKMFDVGGQRSEKRWIHC FEGVTAI IFCVALSAYDLVLAEDDEE
MNRMHESMKLFDSICNNKWFTDTSI ILFLNKKDLFEEKI THSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
YTHFTCATDTKNVQFVFDAVTDV I IKNNLKDCGPF

>Gαi2 L-2R(=L354R) (SEQ ID NO: 34)
MGCTVSAEDKAAAERSKMIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKI IHEDGYSEEECRQYRAVVYSNTIQS
IMAI VKAMGNLQIDFADPSRADDARQLFALSCTAEEQGVLPDDL SGVIRRLWADHGVQACFGRSREYQLNDSAAAYLNDL
ERIAQSDYIPTQQDVLRLTRVKTGTGIVETHFTFKDLHFKMFDVGGQRSEKRWIHC FEGVTAI IFCVALSAYDLVLAEDDEE
MNRMHESMKLFDSICNNKWFTDTSI ILFLNKKDLFEEKI THSPLTICFPEYTGANKYDEAASYIQSKFEDLNKRKDTKEI
YTHFTCATDTKNVQFVFDAVTDV I IKNNLKDCGRF

>GαoB L-2G(=L353G) (SEQ ID NO: 35)
MGCTLSAEEAALERSKAIEKNLKEDGISAAKDVKLLLLGAGESGKSTIVKQMKI IHEDGFSGEDVKQYKPVVYSNTIQS
LAAIVRAMDTLGI EYGD KERKADAKMVC DVVSRMEDTEPFSAE LLSAMMRLWGDSGI QECFNRSREYQLNDSAKYYLDSL
DRIGAADYQPTQDILRLTRVKTGTGIVETHFTFKNLHFR LFDVGGQRSEKRWIHC FEDVTAI IFCVALSGYDQVLHEDET
TNRMHESLKLFD SICNNKWFTDTSI ILFLNKKDIFEEKI KKSPLTICFPEYTGPSAFTEAVAYIQAYESKNKSAHKEIY
THVTCATDTNNIQFVFDAVTDV I IAKNLRGCGY

>GαoB Δ5(=1-349) (SEQ ID NO: 36)
MGCTLSAEEAALERSKAIEKNLKEDGISAAKDVKLLLLGAGESGKSTIVKQMKI IHEDGFSGEDVKQYKPVVYSNTIQS
LAAIVRAMDTLGI EYGD KERKADAKMVC DVVSRMEDTEPFSAE LLSAMMRLWGDSGI QECFNRSREYQLNDSAKYYLDSL
DRIGAADYQPTQDILRLTRVKTGTGIVETHFTFKNLHFR LFDVGGQRSEKRWIHC FEDVTAI IFCVALSGYDQVLHEDET
TNRMHESLKLFD SICNNKWFTDTSI ILFLNKKDIFEEKI KKSPLTICFPEYTGPSAFTEAVAYIQAYESKNKSAHKEIY
THVTCATDTNNIQFVFDAVTDV I IAKNLR

>RLucII (SEQ ID NO: 37)
MTSKVYDPEQRKRMITGPQWWARCKQMNVLDSFINYYDSEKHAENAVIFLHGNATSSYLWRHVPHIEPVARCIIPDLIG
MGKSGKSGNGSYRLLDHYKYLTAWFELNLNLPKKI IFVGHDWGAALAFHYSYEHQDKI KAIVHAESVVDVIBSWDEWPDIE
EDIALIKSEEGEKMVLNNFFVETVLP SKIMRKLEPEEFAAYLEPFKEKGEVRRPTLSWP REIPLVKGGKPDVVQIVRNY
NAYLRASDDL PKMFIESDPGFFSNAIVEGAKKFPNTEFVKVGLHFSQEDAPDEM GKYIKSFVERVLKNEQ

>rGFP: (SEQ ID NO: 38)
MDLAKLGLKEVMPTKINLEGLVGDHAFSMEGVGEGNILEGTQEVKISVTKGAPLPFAFDIVSVAFSYGNRAYTGYPEEIS
DYFLQSFPEGFTYERNIRYQDGGTAIVKSDISLEDGKFI VNVDFKAKDLRRMGPMVQQDIVGMQPSYESMYTNVTSVIGE
CIIAFKLQTKGHFTYHMRTVYKSKKPVETMPLYHFIQHRLVKTNVDTASGVVVQHE TAIAAHSTIKIEGSLP

>endofin's FYVE domain (SEQ ID NO: 39)
QKQPTWVPDSEAPNCMNQC VKFTFTKRRHHCACGKVFCGVCCNRKCKLQYLEKEARVCVVCYETISK

>CAAX sequence; plasma-membrane targeting domain from KRAS (SEQ ID NO: 1)
GKKKKKKSKTKCVIM

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FIG. 9C

>RGS(RGS17;residues 64-210 of SEQ ID NO:17)
IQVLEECQNPTAEEVLSWSQNFDKMMKAPAGRNLFREFLRTEYSEENLLFWLACEDLKKEQNKKVIEEKARMIYEDYISI
LSPKEVSLDSRVREVINRNLLDPNPHMYEDAQLQIYTLMHRDSFPRFLNSQIYKSFVESTAGSSSES

>RGS(RGS19;residues 70-217 of SEQ ID NO:18)
LPSCEVCATPSPPEEVQSWAQSFDKLMHSPAGRSVFRAFLRTEYSEENMLFWLACEELKABANQHVVDEKARLIYEDYVSI
LSPKEVSLDSRVREGINKKMQEPSAHTFDDAQLQIYTLMHRDSYPRFLSSPTYRALLLQGPSQSSSEA

>RGS(RGS20;residues 242-388 of SEQ ID NO:19)
LPTWEESPAPTL EEVNAWAQSFDKLMVTPAGRNAFREFLRTEFSEENMLFWMA CEELKKEANKNIEEKARIYEDYISI
LSPKEVSLDSRVREVINRNMVEPSQHIFDDAQLQIYTLMHRDSYPRFMNSAVYKDLLQSLSEKSIEA

FIG. 9D