FIG.1A

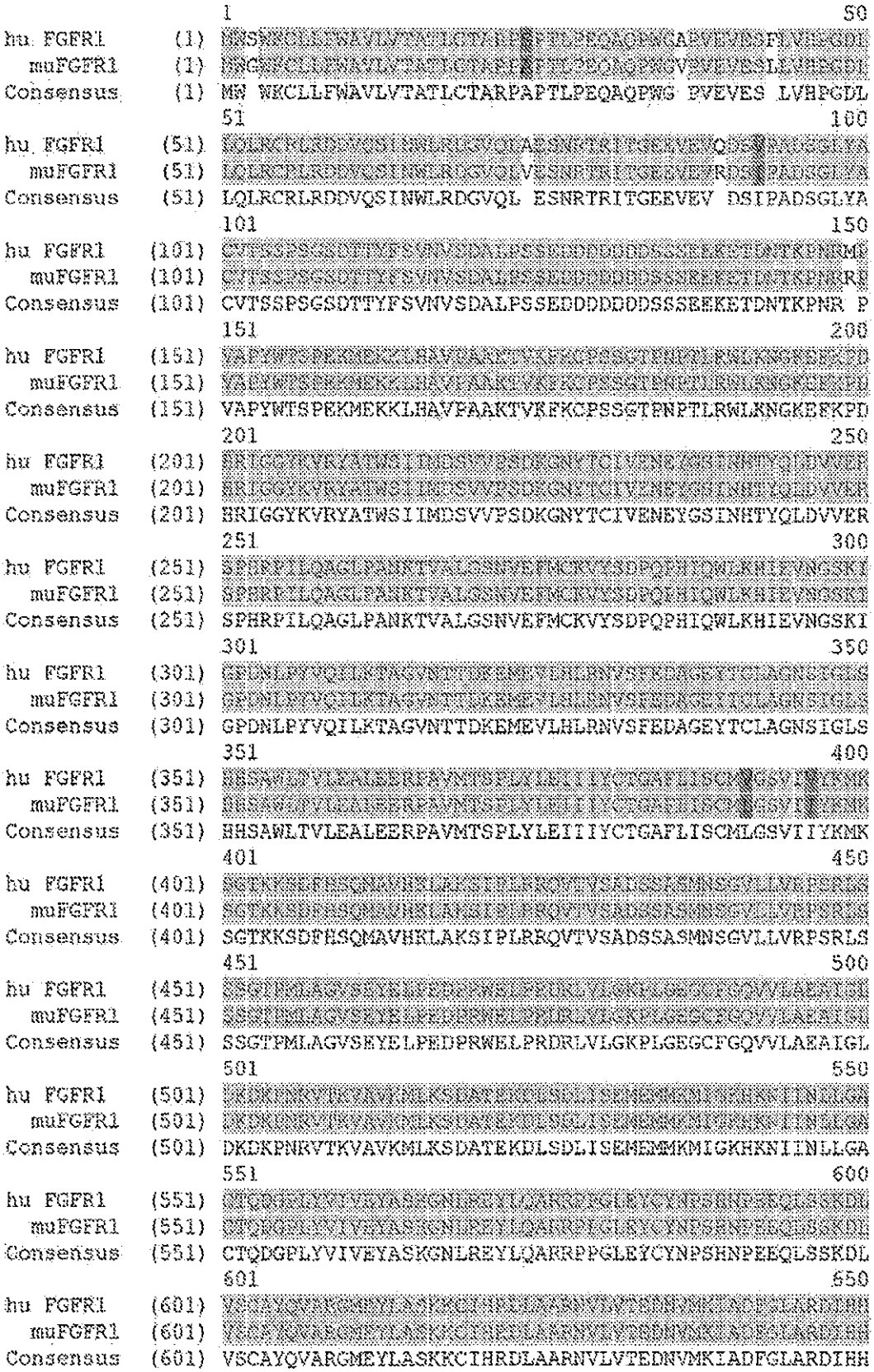

1 50
hu FGFR1 (1)
muFGFR1 (1)
Consensus (1) MW WKCLLFWAVLVTATLCTARPAPTLPEQAQPWG PVEVES LVHPGDL
51 100
hu FGFR1 (51)
muFGFR1 (51)
Consensus (51) LQLRCRLRDDVQSINWLRDGVQL ESNRTRITGEEVEV QDSIPADSGLYA
101 150
hu FGFR1 (101)
muFGFR1 (101)
Consensus (101) CVTSSPSGSDTTYFSVNVSDALPSSEDDDDDDDSSSEEKETDNTKPNR P
151 200
hu FGFR1 (151)
muFGFR1 (151)
Consensus (151) VAPYWTSPEKMEKKLHAVPAAKTVKFKCPSSGTPNPTLRWLKNGKEFKPD
201 250
hu FGFR1 (201)
muFGFR1 (201)
Consensus (201) HRIGGYKVRYATWSIIMDSVVPSDKGNYTCIVENEYGSINHTYQLDVVER
251 300
hu FGFR1 (251)
muFGFR1 (251)
Consensus (251) SPHRPILQAGLPANKTVALGSNVEFMCKVYSDPQPHIQWLKHIEVNGSKI
301 350
hu FGFR1 (301)
muFGFR1 (301)
Consensus (301) GPDNLPYVQILKTAGVNTTDKEMEVLHLRNVSFEDAGEYTCLAGNSIGLS
351 400
hu FGFR1 (351)
muFGFR1 (351)
Consensus (351) HHSAWLTVLEALEERPAVMTSPLYLEIIIYCTGAFLISCMVGSVIVYKMK
401 450
hu FGFR1 (401)
muFGFR1 (401)
Consensus (401) SGTKKSDFHSQMAVHKLAKSIPLRRQVTVSADSSASMNSGVLLVRPSRLS
451 500
hu FGFR1 (451)
muFGFR1 (451)
Consensus (451) SSGTPMLAGVSEYELPEDPRWELPRDRLVLGKPLGEGCFGQVVLAEAIGL
501 550
hu FGFR1 (501)
muFGFR1 (501)
Consensus (501) DKDKPNRVTKVAVKMLKSDATEKDLSDLISEMEMMKMIGKHKNIINLLGA
551 600
hu FGFR1 (551)
muFGFR1 (551)
Consensus (551) CTQDGPLYVIVEYASKGNLREYLQARRPPGLEYCYNPSHNPEEQLSSKDL
601 650
hu FGFR1 (601)
muFGFR1 (601)
Consensus (601) VSCAYQVARGMEYLASKKCIHRDLAARNVLVTEDNVMKIADFGLARDIHH

FIG.1B

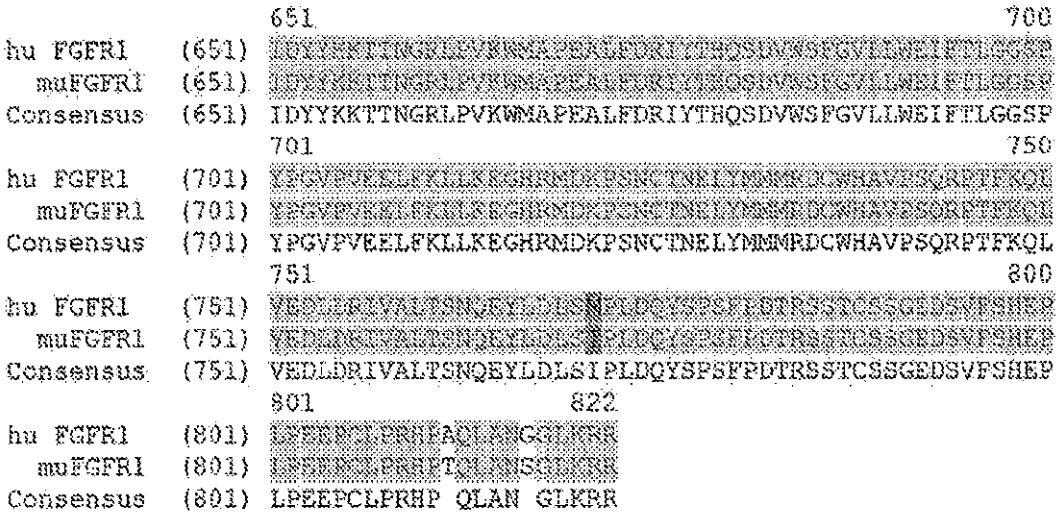

651 700
hu FGFR1 (651)
muFGFR1 (651)
Consensus (651) IDYYKKTTNGRLPVKWMAPEALFDRIYTHQSDVWSFGVLLWEIFTLGGSP
701 750
hu FGFR1 (701)
muFGFR1 (701)
Consensus (701) YPGVPVEELFKLLKEGHRMDKPSNCTNELYMMMRDCWHAVPSQRPTFKQL
751 800
hu FGFR1 (751)
muFGFR1 (751)
Consensus (751) VEDLDRIVALTSNQEYLDLSIPLDQYSPSFPDTRSSTCSSGEDSVFSHEP
801 822
hu FGFR1 (801)
muFGFR1 (801)
Consensus (801) LPEEPCLPRHP QLAN GLKRR

FIG. 2A

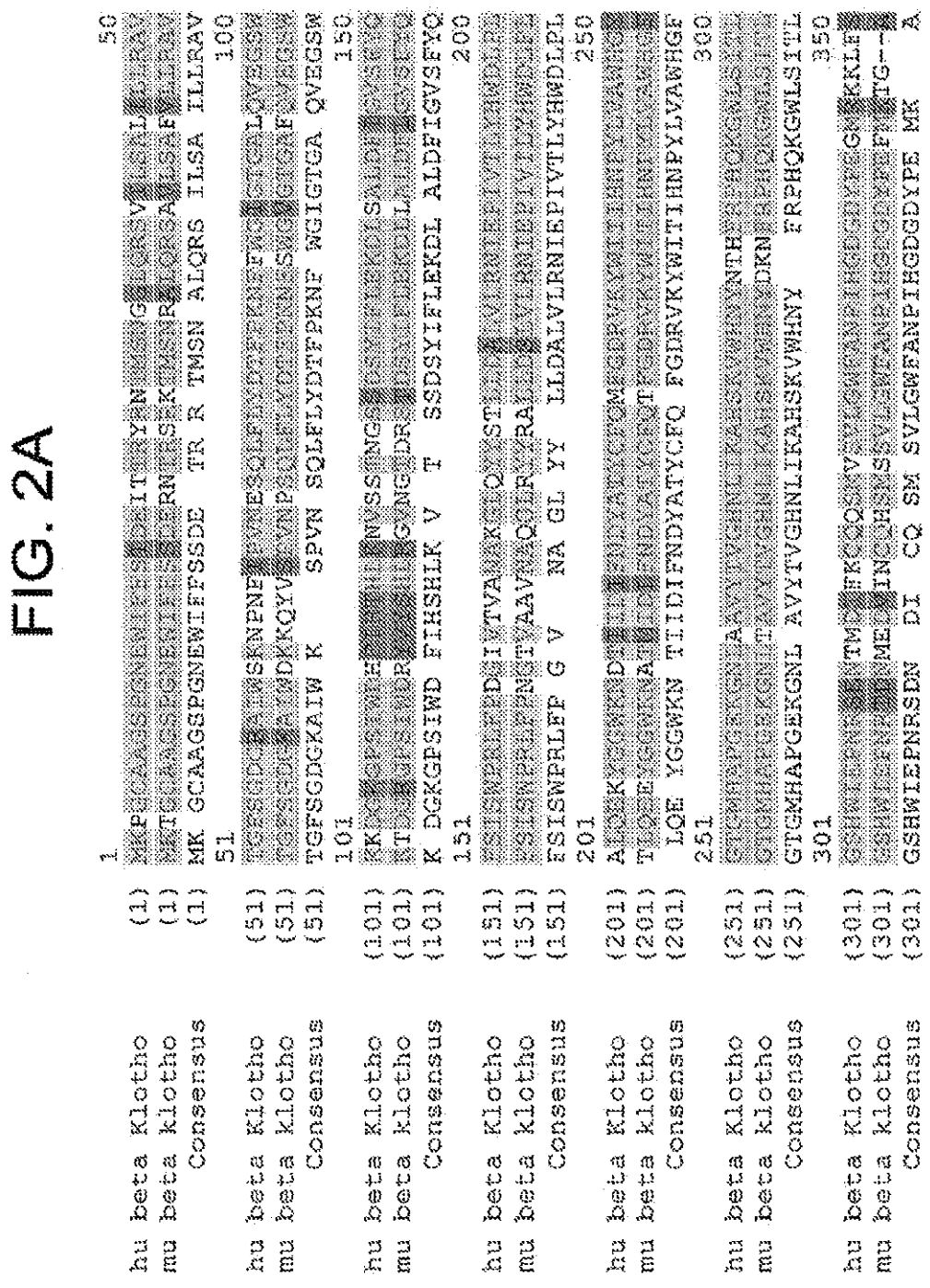


FIG. 2B

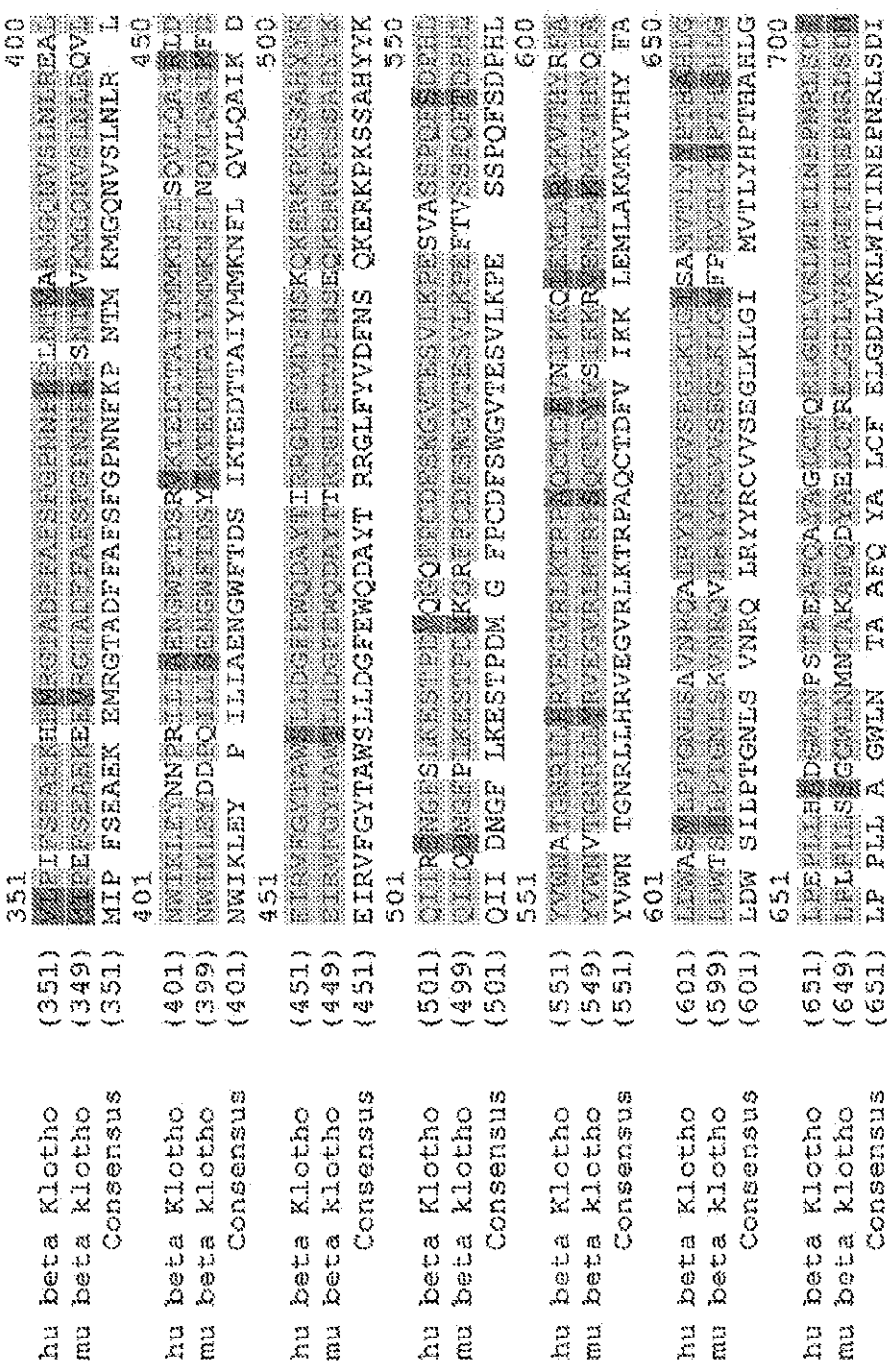


FIG. 2C

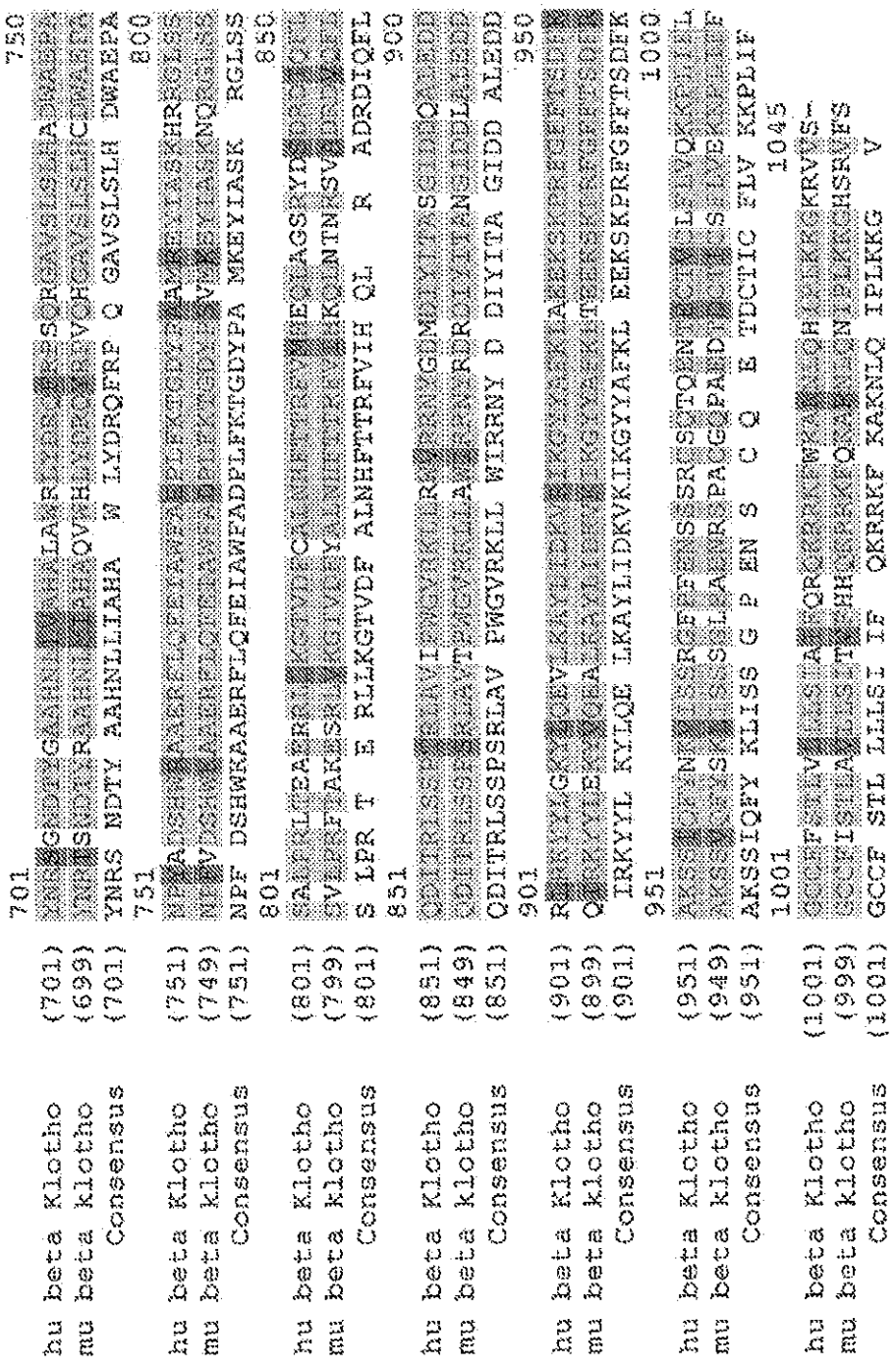


FIG. 3A

AM-1 Parental-Unstained

DB120707-AM1 Unstained

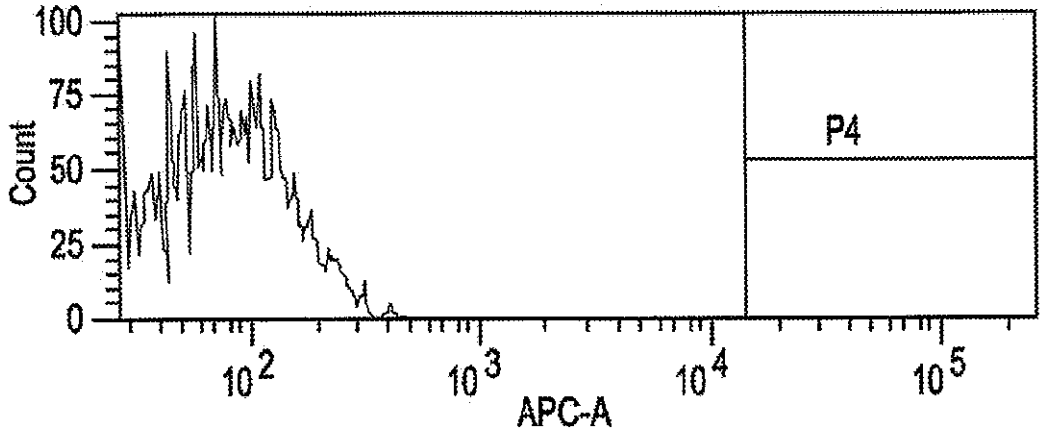


FIG. 3B

AM-1 /bKlotho +FGFR1 pool 3 - Unstained

DB120707-Pool3 Unstained

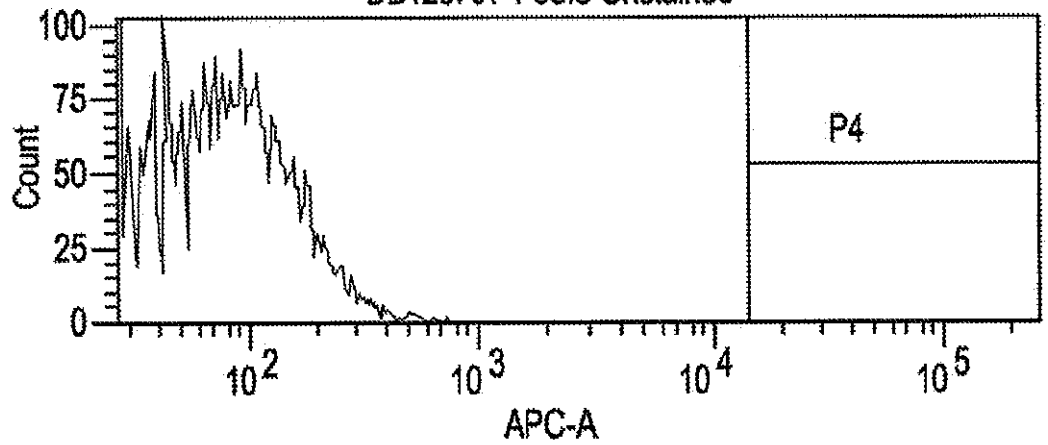


FIG. 3C

CHO/bKlotho+FGFR1 pool 5- Unstained

DB120707-Pool5 Unstained

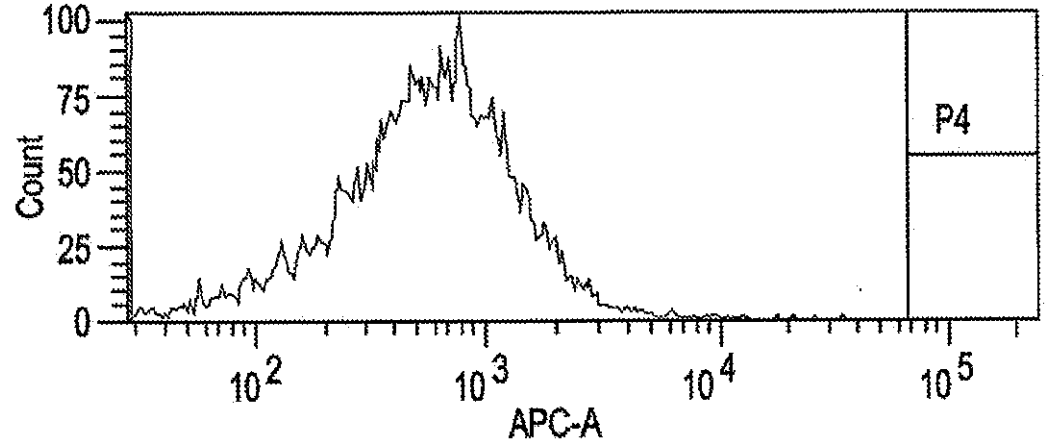


FIG. 3D

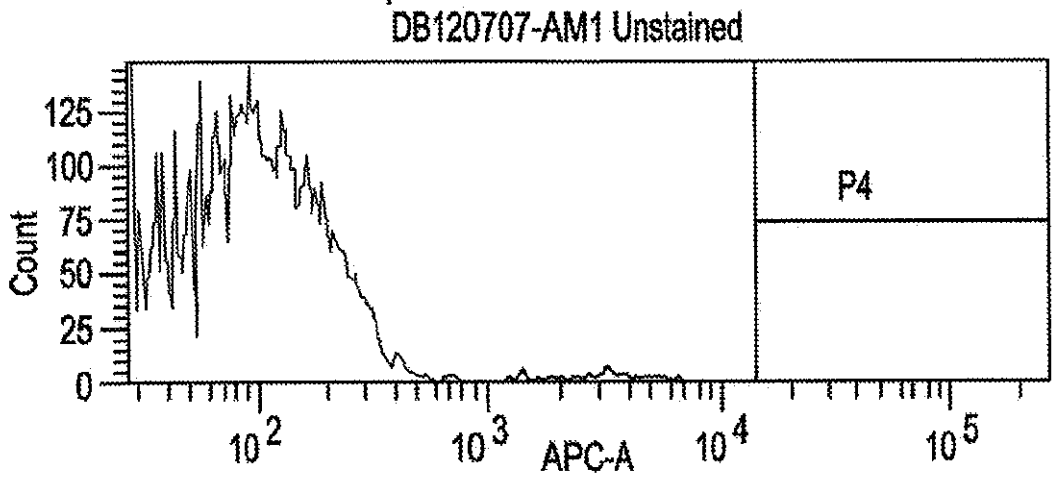


FIG. 3E

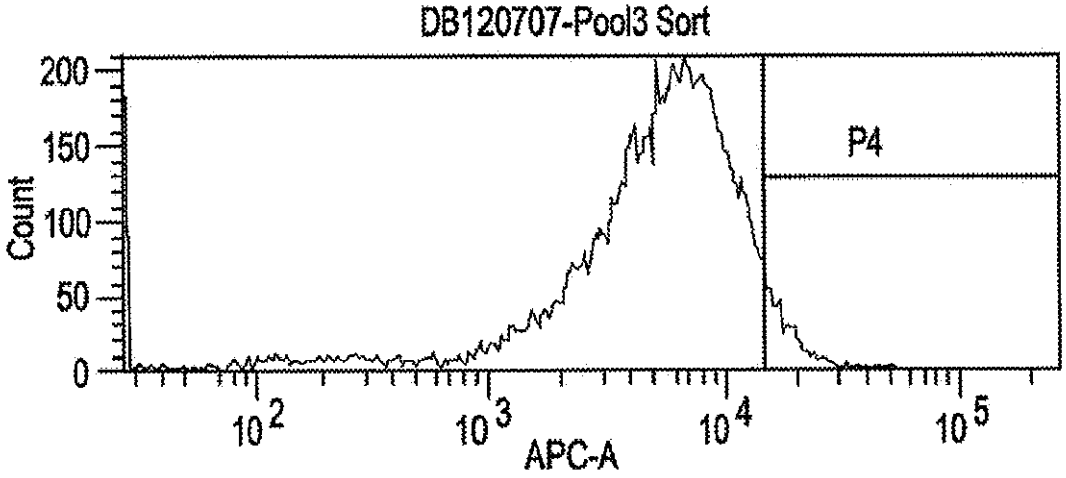


FIG. 3F

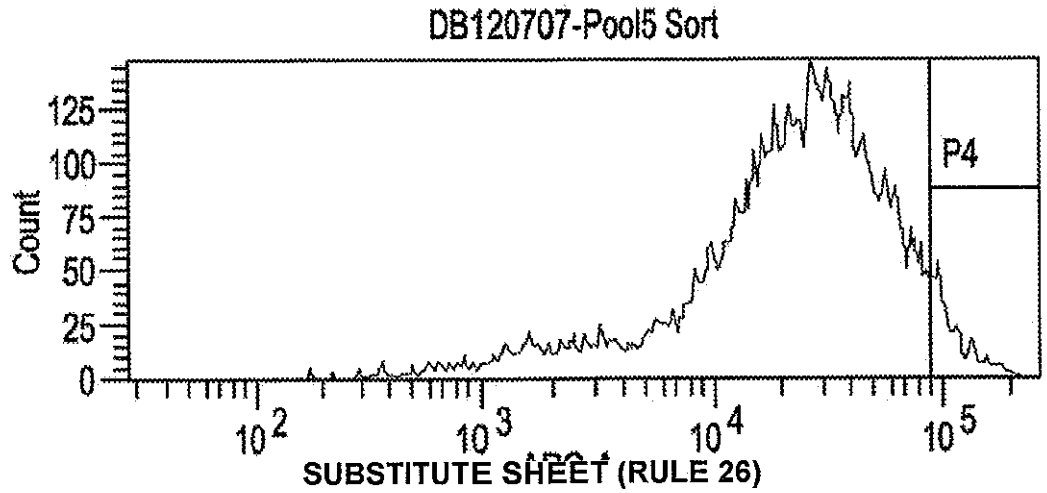


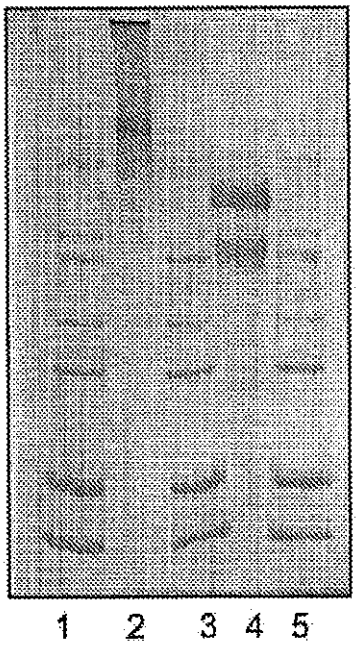
FIG. 4

DPSPTLPEQAQPWGAPVEVESFLVHPGDLLQLRCRLRDDVQSINWLRDGVQL
AESNRTRITGEEVEVQDSVPADSGLYACVTSSPSGSDTTYFSVNVSDALPSS
EDDDDDDDSSSEEKETDNTKPNRMPVAPYWTSPEKMEKKLHAVPAAKTVKFK
CPSSGTPNPTLRWLKNGKEFKPDHRIGGYKVRYATWSIIMDSVVPSDKGNYT
CIVENEYGSINHTYQLDVVERSPHRPILQAGLPANKTVALGSNVEFMCKVYS
DPQPHIQWLKHIEVNGSKIGPDNLPYVQILKTAGVNTTDKEMEVLHLRNVSF
EDAGEYTCLAGNSIGLSHHSAWLTVLEALEERPAVMTSPLY*ggggg*dkthtc
ppcpapellggpsvflfppkpkdtlmisrtpevtcVvvdvshedpevkfnwy
vdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeyKckvsnkalpa
piektiskakgqprepqvytlppsrdeltknqvsltclvkgfypsdiavewE
sngqpennykttppvldsdgsfflyskltvdksrwqqgnvfscsvmhealhn
hytqkslslspgk

FIG. 5

```
FSGDGRAI WSKNPNFTPV NESQLFLYDT FPKNFFWGIG TGALQVEGSW
KKDGKGPSIW DHFIHTHLKN VSSTNGSSDS YIFLEKDLSA LDFIGVSFYQ
FSISWPRLFP DGIVTVANAK GLQYYSTLLD ALVLRNIEPI VTLYHWDLPL
ALQEKYGGWK NDTIIDIFND YATYCFQMFG DRVKYWITIH NPYLVAWHGY
GTGMHAPGEK GNLAAVYTVG HNLIKAHSKV WHNYNTHFRP HQKGWLSITL
GSHWIEPNRS ENTMDIFKCQ QSMVSVLGWF ANPIHGDGDY PEGMEKKLFS
VLPIFSEAEK HEMRGTADFF AFSFGPNNFK PLNTMAKMGQ NVSLNLREAL
NWIKLEYNNP RILIAENGWF TDSRVKTEDT TAIYMMKNFL SQVLQAIRLD
EIRVFGYTAW SLLDGFEWQD AYTIRRGLFY VDFNSKQKER KPKSSAHYYK
QIIRENGFSL KESTPDVQGQ FPCDFSWGVT ESVLKPESVA SSPQFSDPHL
YVTWNATGNRL LHRVEGVRLK TRPAQCTDFV NIKKQLEMLA RMKVTHYRFA
LDWASVLPTG NLSAVNRQAL RYYRCVVSEG LKLGISAMVT LYYPTHAHLG
LPEPLLHADG WLNPSTAEAF QAYAGLCFQE LGDLVKLWIT INEPNRLSDI
YNRSGNDTYG AAHNLLVAHA LAWRLYDRQF RPSQRGAVSL SLHADWAEPA
NPYADSHWRA AERFLQFEIA WFAEPLFKTG DYPAAMREYI ASKHRRGLSS
SALPRLTEAE RRLLKGTVDF CALNHFTTRF VMHEQLAGSR YDSDRDIQFL
QDITRLSSPT RLAVIPWGVR KLLRWVRRNY GDMDIYITAS GIDDQALEDD
RLRKYYLGKY LQEVLKAYLI DKVRIKGYYA FKLAEEKSKP RFGFFTSDFK
AKSSIQFYNK VISSRGFPFE NSSSRCSQTQ ENTECTVCLF LVQKKP
ggggqdkthtcppcpapellggppsvflfppkpkdtlmisrtpevtcvvvdvshe
dpevkfnwyvdgvevhnaktkpreeqynstyrvvsvltvlhqdwlngkeykckv
snkalpapiektiskakgqprepqvytlppsrdeltknqvsltclvkgfypsdi
avewesngqpennyktppvldsdgsfflyskltvdksrwqqgnvfscsvmhea
lhnhytqkslslspgk
```

FIG. 6



1. Mol. wt. markers
2. Heterodimer, non-reducing
3. Stds
4. Heterodimer, reducing
5. Mol. wt. markers

FIG. 7A

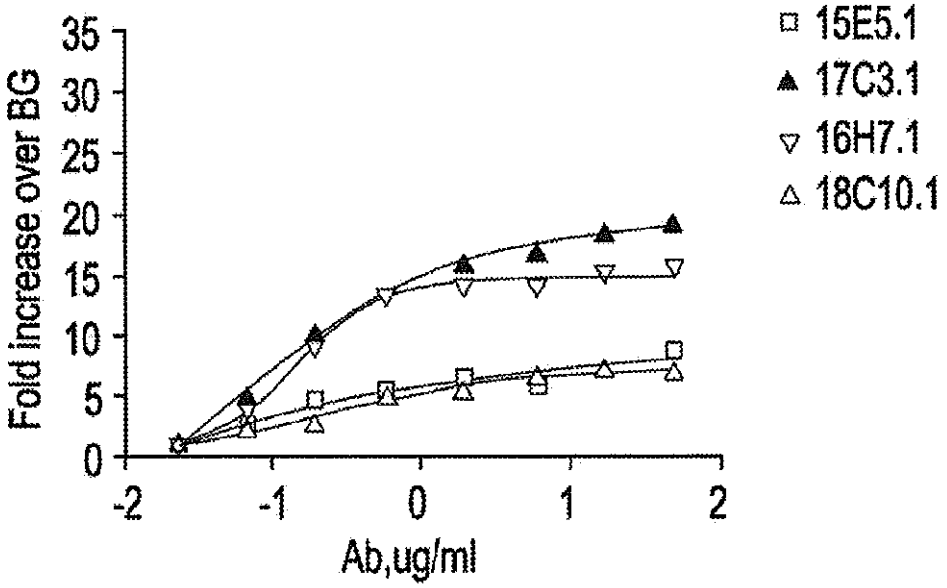

Fold increase over BG
35
30
25
20
15
10
5
0
-2
-1
0
1
2
Ab,ug/ml
15E5.1
17C3.1
16H7.1
18C10.1

FIG. 7B

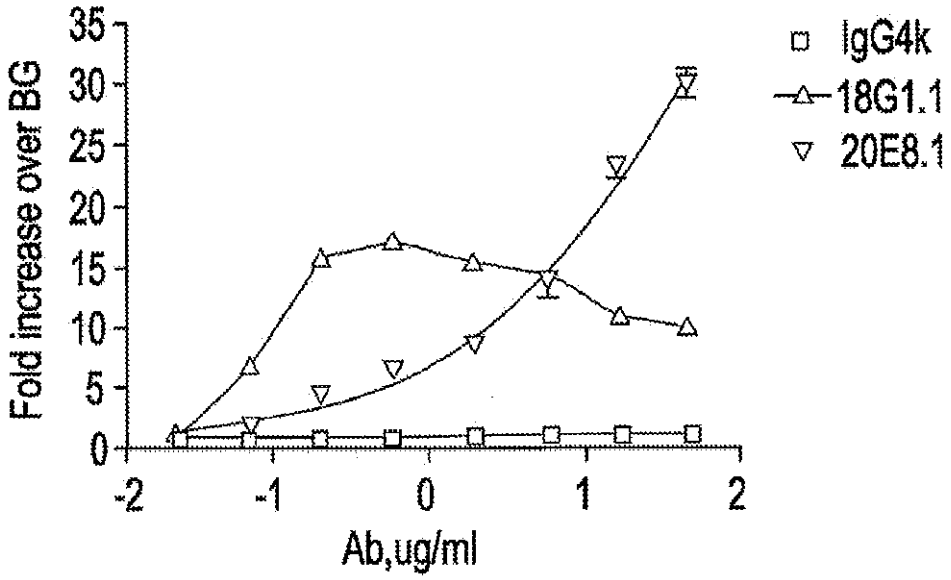

Fold increase over BG
35
30
25
20
15
10
5
0
-2
-1
0
1
2
Ab,ug/ml
IgG4k
18G1.1
20E8.1

FIG. 7C

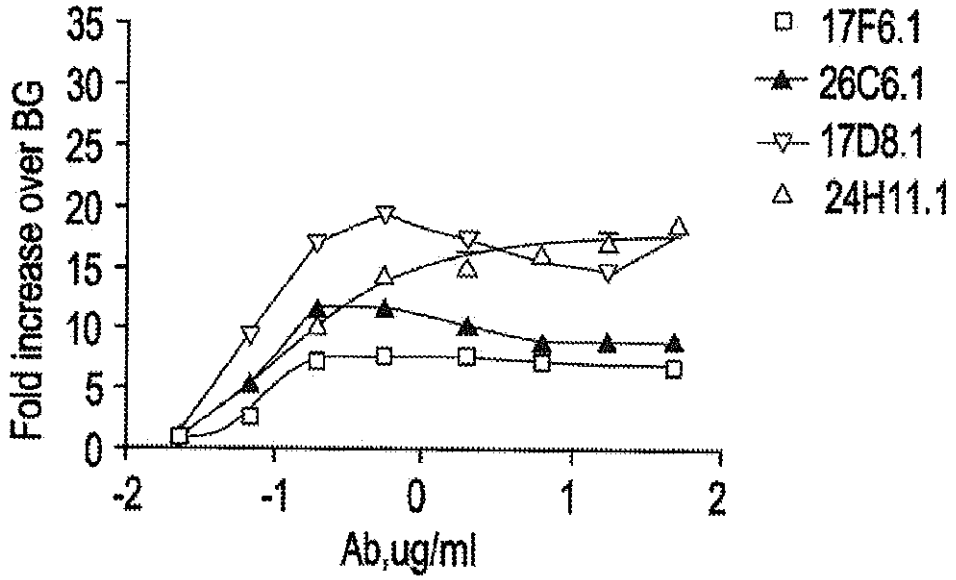

Fold increase over BG
35
30
25
20
15
10
5
0
-2
-1
0
1
2
Ab,ug/ml
17F6.1
26C6.1
17D8.1
24H11.1

FIG. 7D

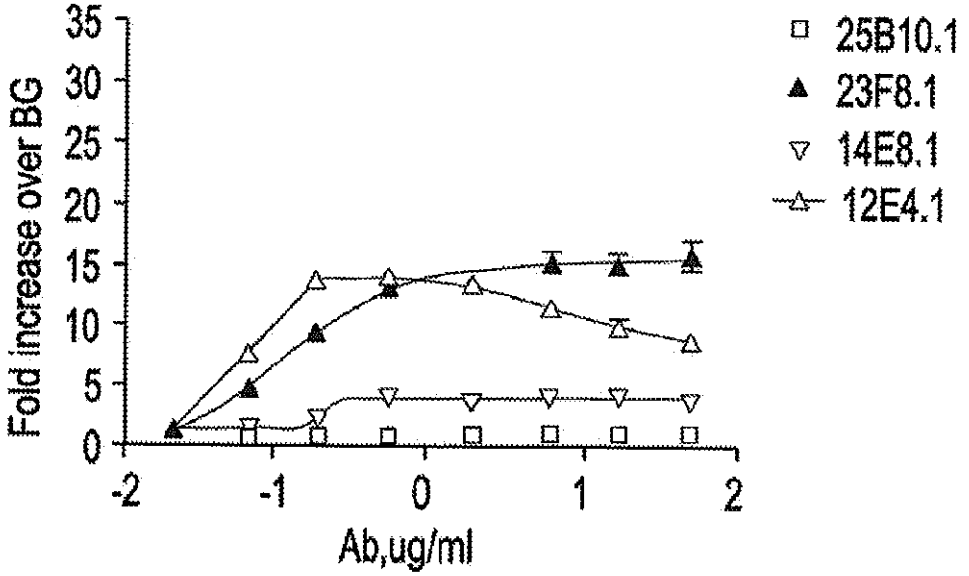

Fold increase over BG
35
30
25
20
15
10
5
0
-2
-1
0
1
2
Ab,ug/ml
25B10.1
23F8.1
14E8.1
12E4.1

FIG. 8A

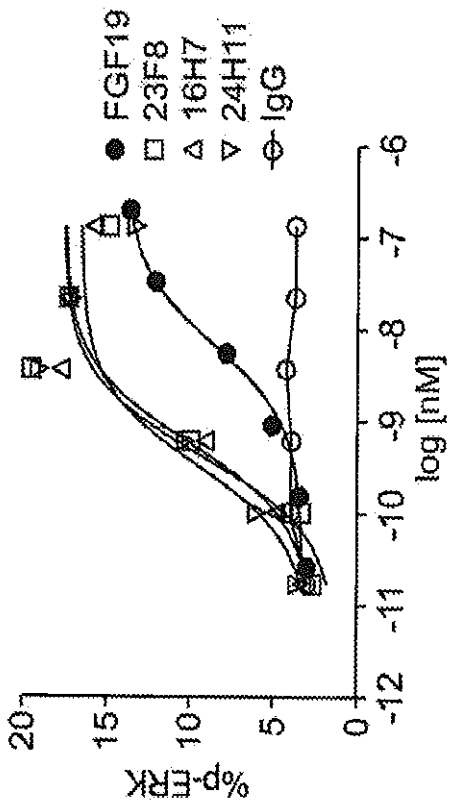


FIG. 8B

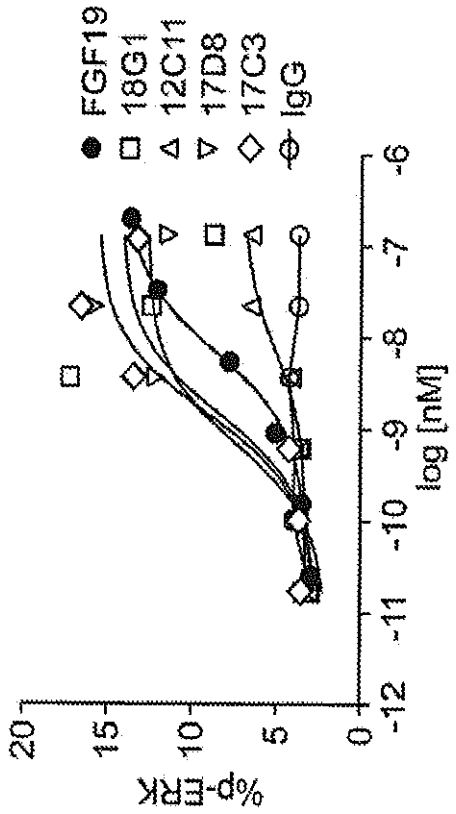
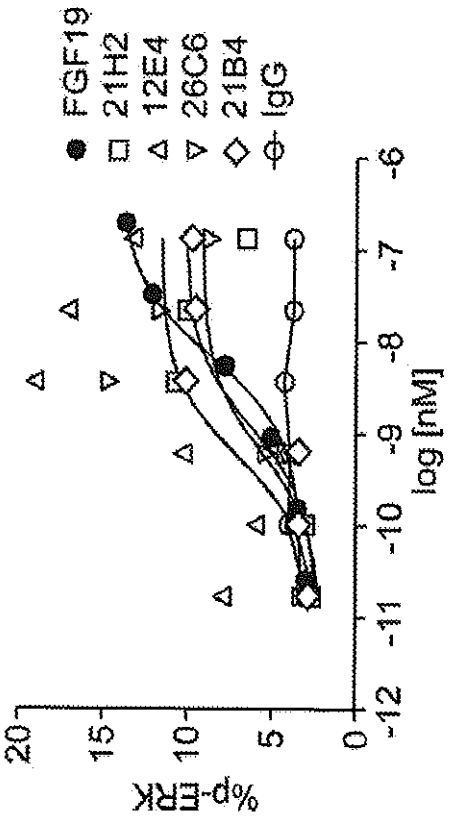


FIG. 8C



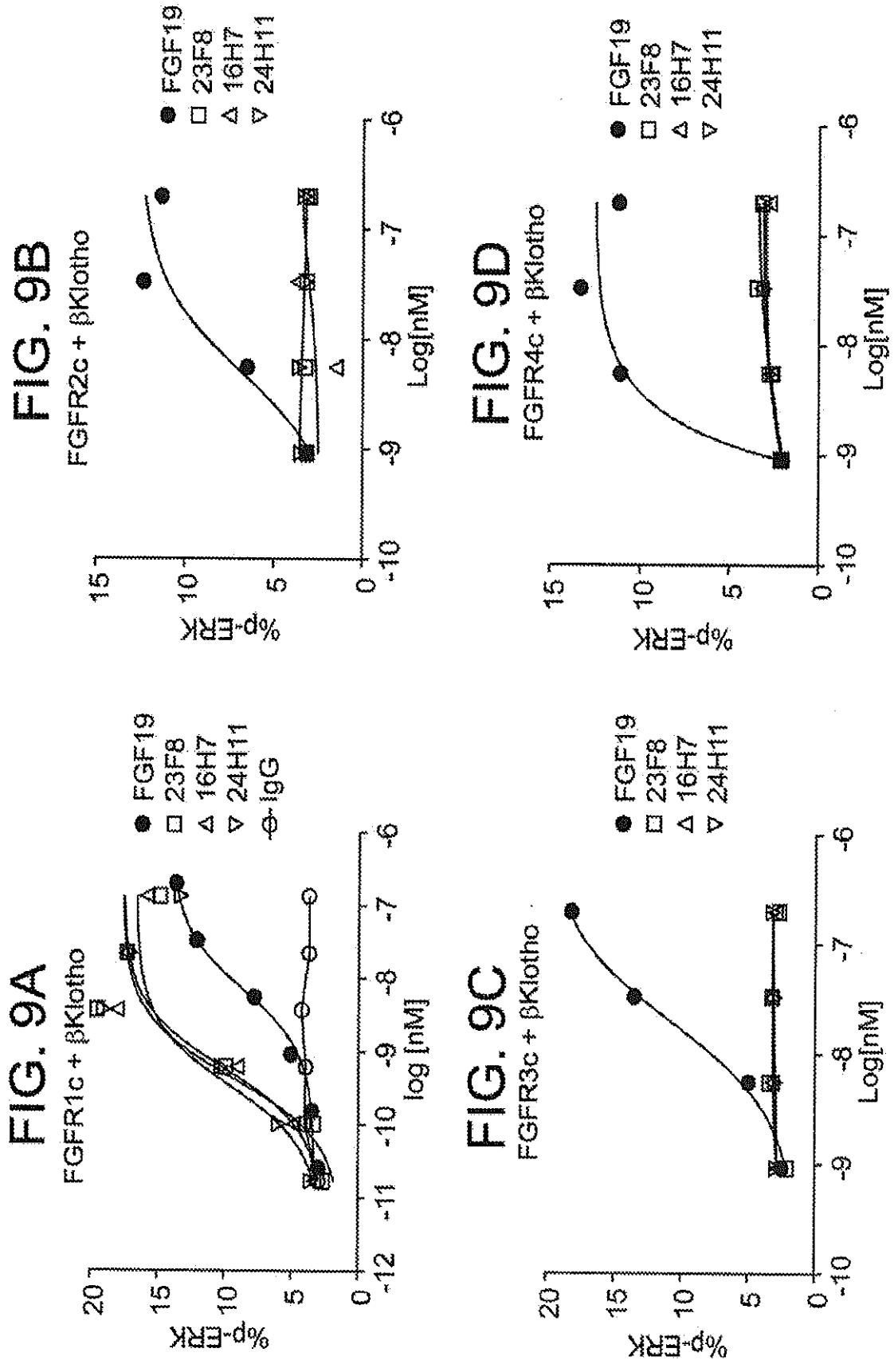

FIG. 9A
FGFR1c + βKlotho
FGF19
23F8
16H7
24H11
IgG
%p-ERK
log [nM]
FIG. 9B
FGFR2c + βKlotho
FGF19
23F8
16H7
24H11
%p-ERK
Log[nM]
FIG. 9C
FGFR3c + βKlotho
FGF19
23F8
16H7
24H11
%p-ERK
Log[nM]
FIG. 9D
FGFR4c + βKlotho
FGF19
23F8
16H7
24H11
%p-ERK
Log[nM]

FIG. 10A

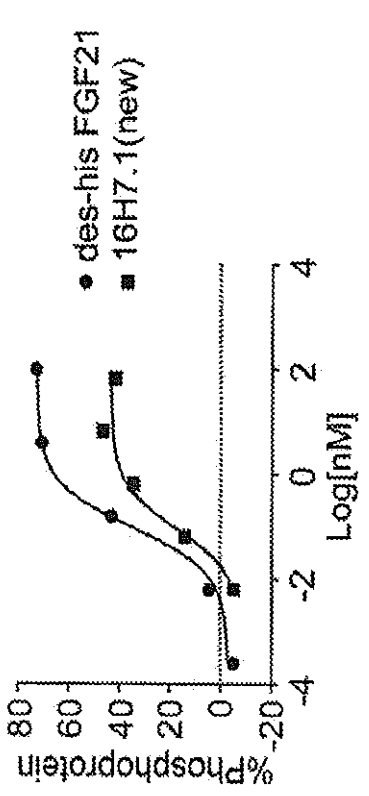


FIG. 10B

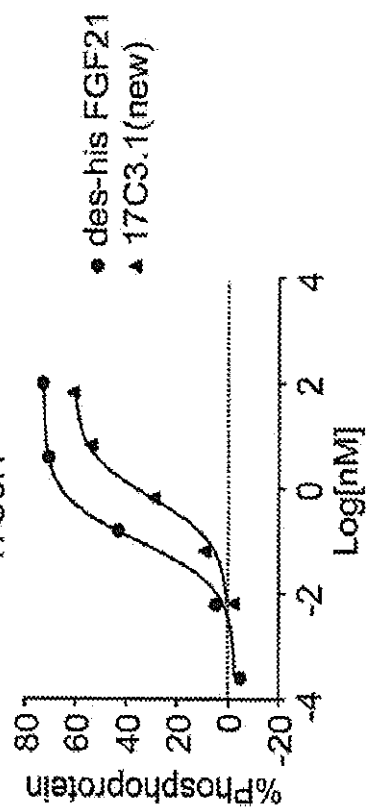


FIG. 10C

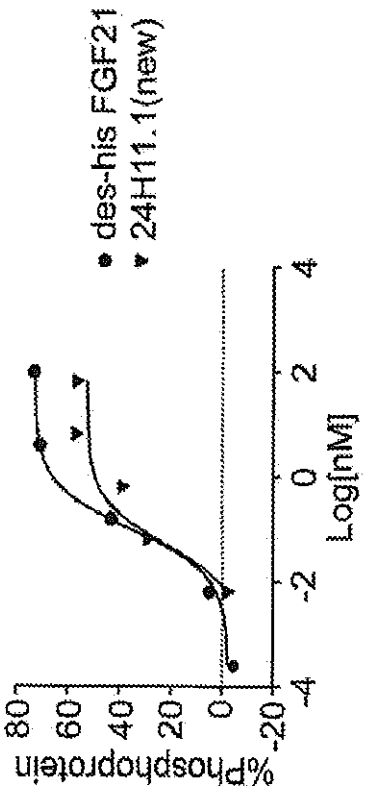


FIG. 10D

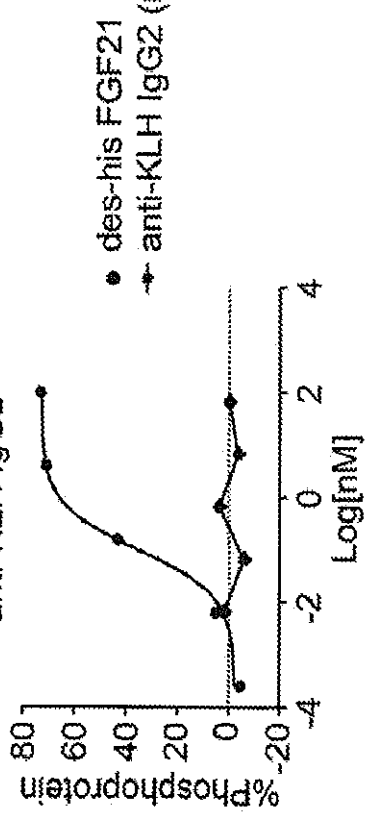


FIG. 11A

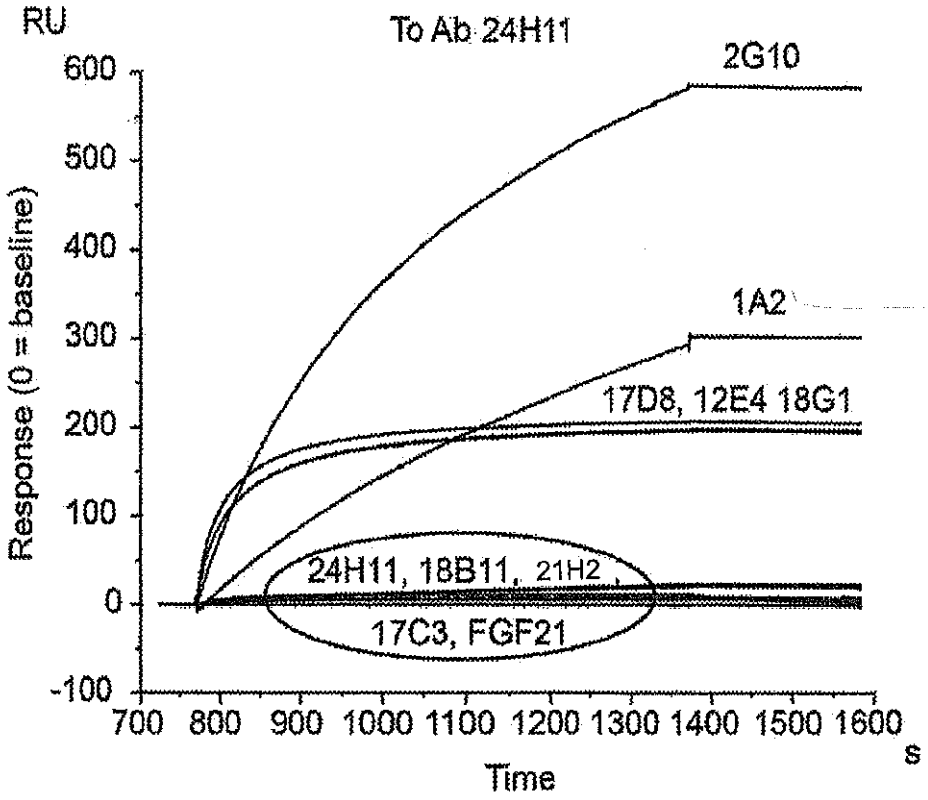

RU
To Ab 24H11
2G10
1A2
17D8, 12E4 18G1
24H11, 18B11, 21H2,
17C3, FGF21
Response (0 = baseline)
600
500
400
300
200
100
0
-100
700 800 900 1000 1100 1200 1300 1400 1500 1600
s
Time

FIG. 11B

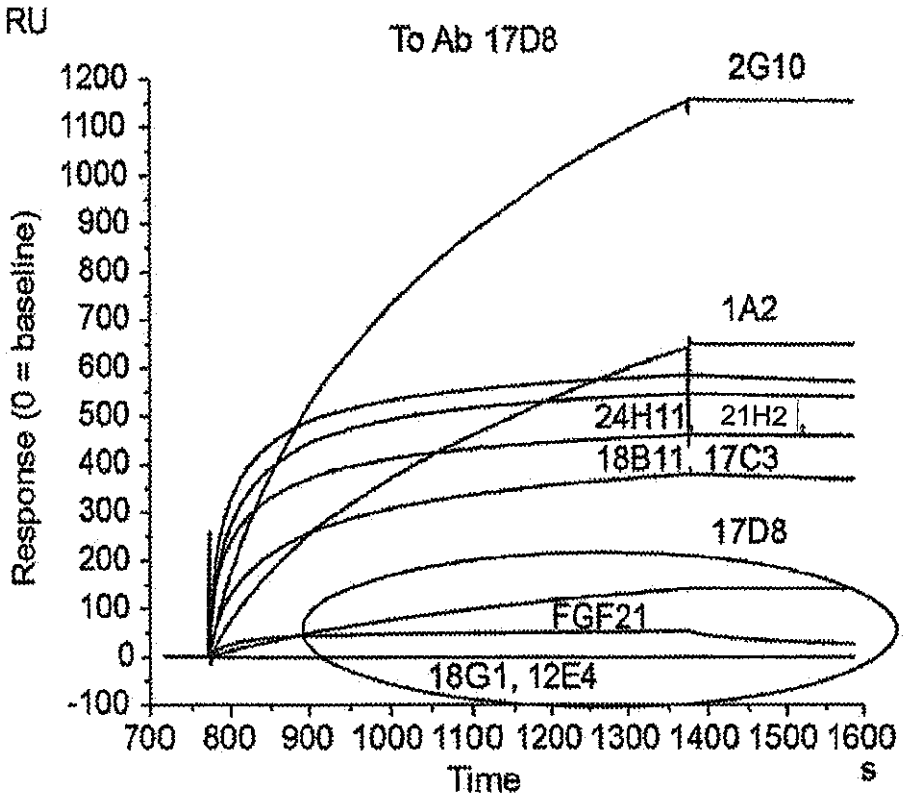

RU
To Ab 17D8
2G10
1A2
24H11
21H2
18B11, 17C3
17D8
FGF21
18G1, 12E4
Response (0 = baseline)
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
700
800
900
1000
1100
1200
1300
1400
1500
1600
Time
s

FIG. 11C

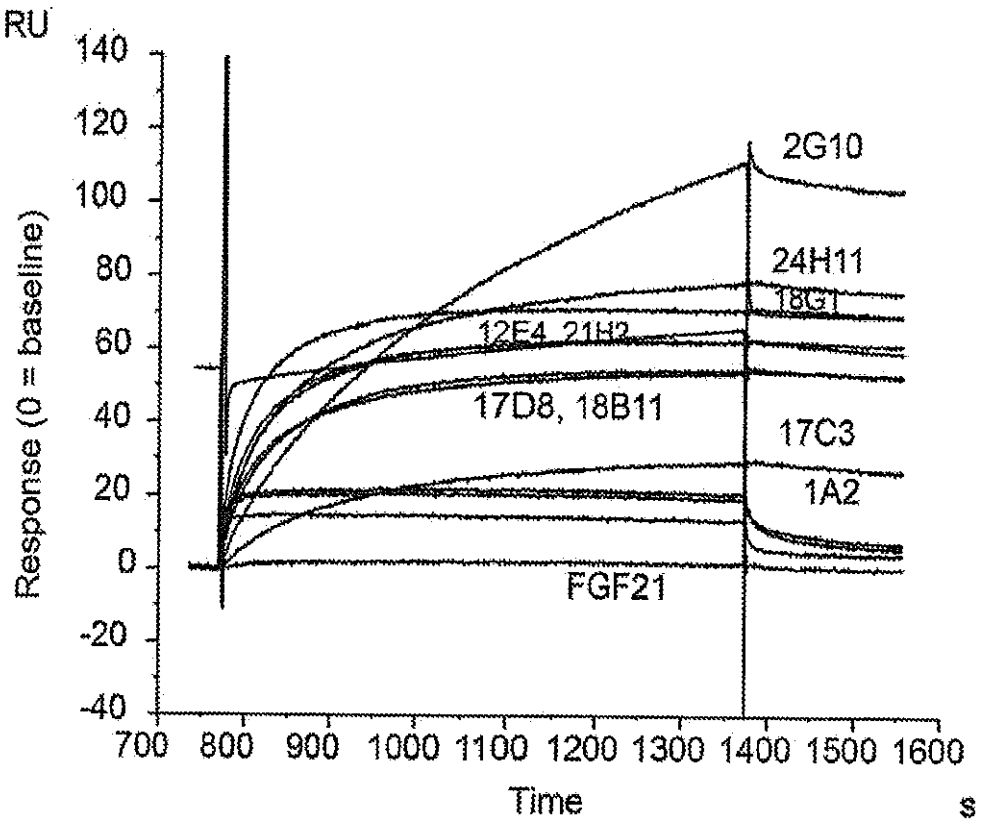

RU
140
120
100
80
60
40
20
0
-20
-40
Response (0 = baseline)
2G10
24H11
18G1
12E4, 21H2
17D8, 18B11
17C3
1A2
FGF21
700 800 900 1000 1100 1200 1300 1400 1500 1600
Time
s

FIG. 11D

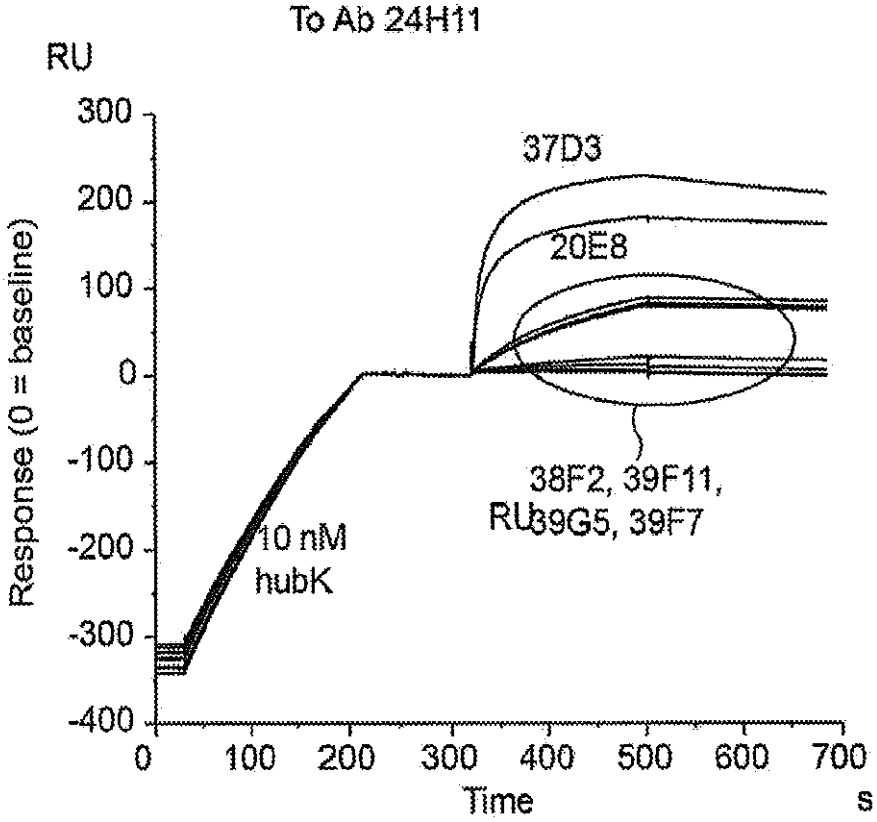

To Ab 24H11
RU
300
200
100
0
-100
-200
-300
-400
Response (0 = baseline)
37D3
20E8
38F2, 39F11,
RU39G5, 39F7
10 nM
hubK
0
100
200
300
400
500
600
700
Time
s

FIG. 11E

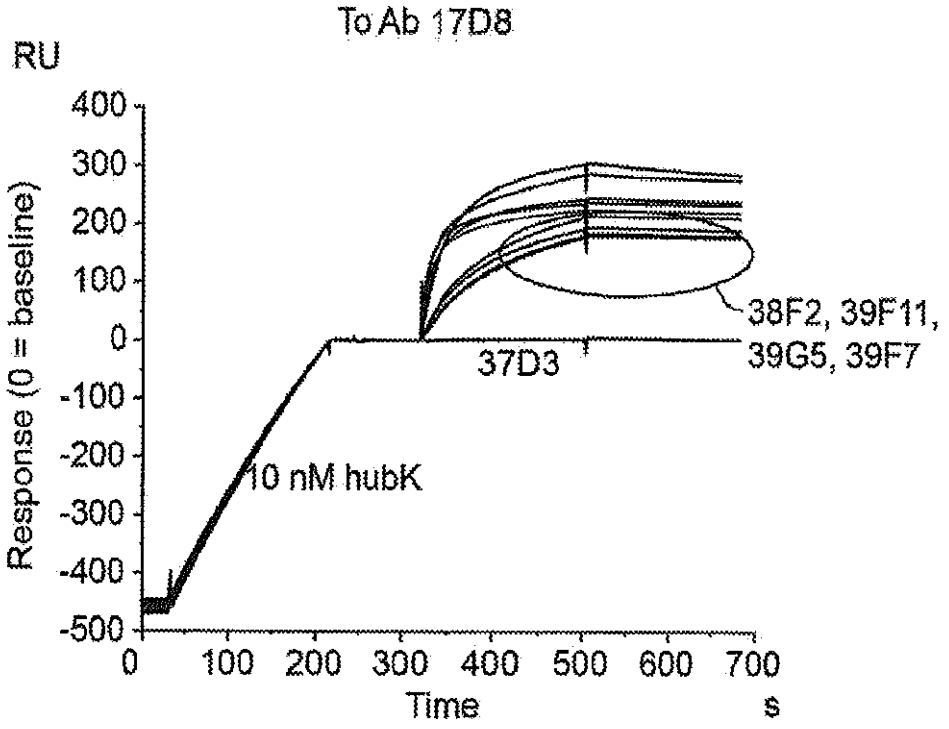

To Ab 17D8
RU
400
300
200
100
0
-100
-200
-300
-400
-500
Response (0 = baseline)
10 nM hubK
37D3
38F2, 39F11,
39G5, 39F7
0
100
200
300
400
500
600
700
Time
s

FIG. 11F

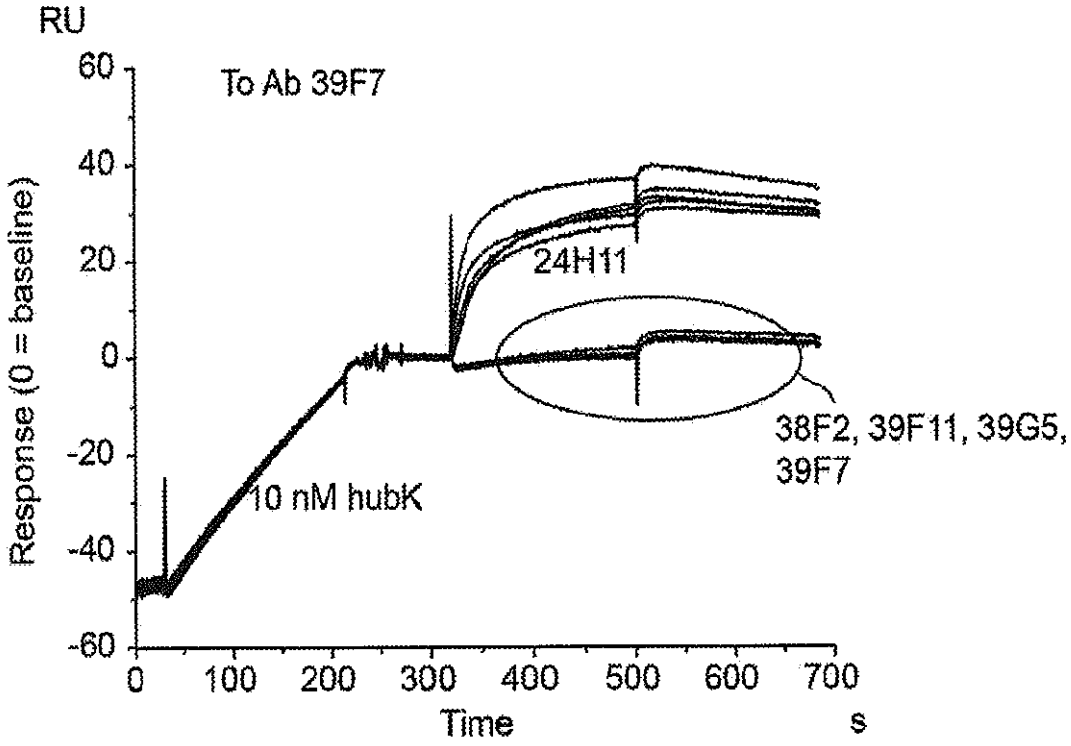

RU
60
40
20
0
-20
-40
-60
Response (0 = baseline)
To Ab 39F7
24H11
38F2, 39F11, 39G5,
39F7
10 nM hubK
0
100
200
300
400
500
600
700
Time
s

FIG. 11G

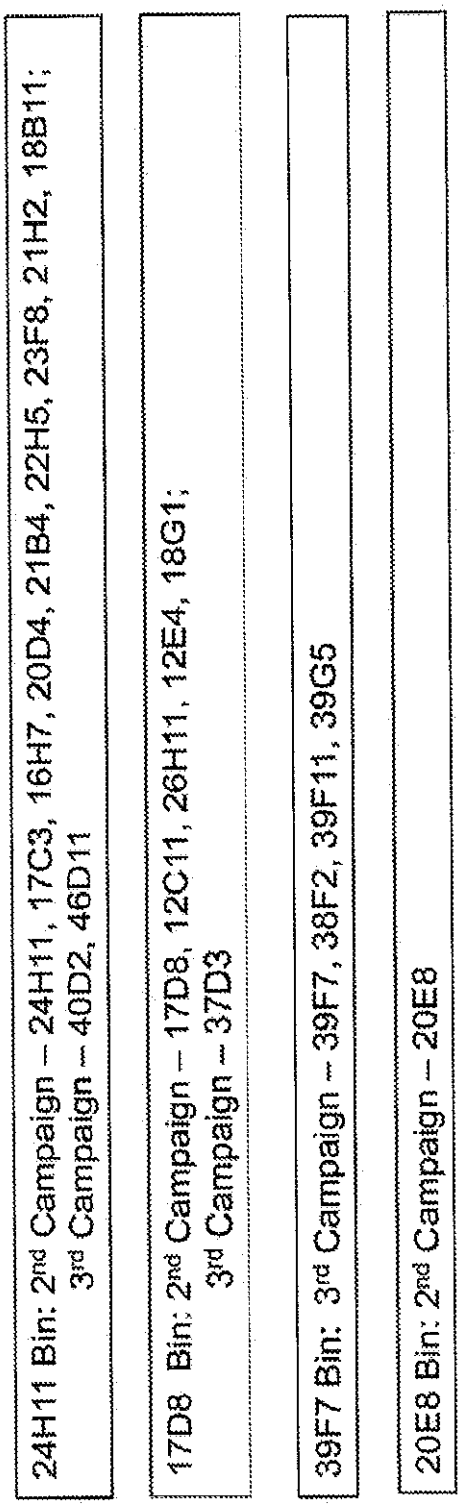

Epitope Binning Summary
24H11 Bin: 2nd Campaign – 24H11, 17C3, 16H7, 20D4, 21B4, 22H5, 23F8, 21H2, 18B11;
3rd Campaign – 40D2, 46D11
17D8 Bin: 2nd Campaign – 17D8, 12C11, 26H11, 12E4, 18G1;
3rd Campaign – 37D3
39F7 Bin: 3rd Campaign – 39F7, 38F2, 39F11, 39G5
20E8 Bin: 2nd Campaign – 20E8

FIG. 12

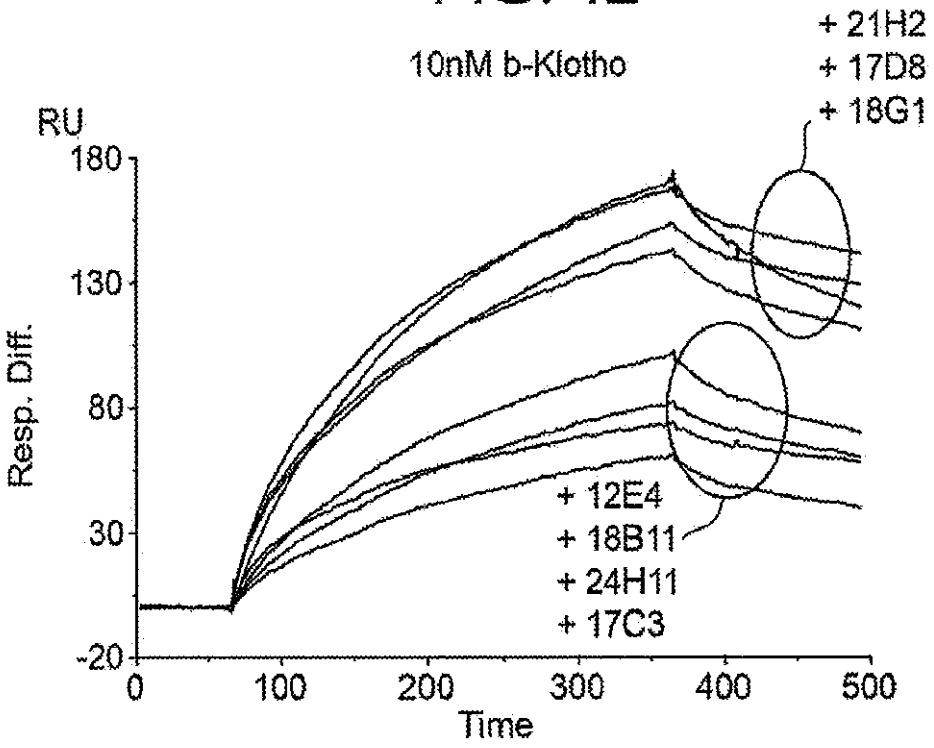

10nM b-Klotho
+ 21H2
+ 17D8
+ 18G1
RU
180
130
80
30
-20
Resp. Diff.
+ 12E4
+ 18B11
+ 24H11
+ 17C3
0
100
200
300
400
500
Time

FIG. 13A

Light chain			
	Germline	Germline	FR1
			DIQMTQSPSSLSASVGDRVTITC
20D4	VK1|A30	JK4	---L---------I------
	Germline	Germline	FR1
			DIQMTQSPSSVSASVGDRVTITC
46D11	VK1|L5	JK5	----------
	Germline	Germline	FR1
			DIVMTQTPLSLSVTPGQPASISC
40D2=36F2=39C2	VK2|A18	JK1	-F----------
	Germline	Germline	FR1
			DIVMTQSPLSLPVTPGEPASISC
37D3	VK2|A19	JK2	----------
	Germline	Germline	FR1
			DIVMTQSPLSLPVTPGEPASISC
18B11 LC#1	VK2|A19	JK3	----------
	Germline	Germline	FR1
			EIVLTQSPGTLSLSPGERATLSC
12C11	VK3|A27	JK4	----------
18G1	VK3|A27	JK4	----------
17D8	VK3|A27	JK4	----------
21B4	VK3|A27	JK4	----------
21H2	VK3|A27	JK4	----------
26H11	VK3|A27	JK4	----------
12E4	VK3|A27	JK4	----------
39F7=47E3=38F2	VK3|A27	JK4	----------
39F11=41H5=37G3=39G8	VK3|A27	JK4	----------
39G5	VK3|A27	JK4	----------
	Germline	Germline	FR1
			EIVMTQSPATLSVSPGERATLSC
18B11 LC#2	VK3|L2	JK1	----------
	Germline	Germline	FR1
			SYVLTQPPSVSVAPGKTARITC
16H7=23F8	VL3|3h	JL3	----------Q------
24H11	VL3|3h	JL3	----------Q------
22H5	VL3|3h	JL3	----------Q------
17C3	VL3|3h	JL3	----------Q------

FIG. 13B

Heavy chain			
	Germline	Germline	FR1
			QVQLVQSGAEVKKPGASVKVSCKVSGY TLT
20D4	VH1|124	JH6	----------
	Germline	Germline	FR1
			QVTLKESGPVLVKPTETLTLTCTVSGFSL S
17C3	VH2|226	JH6	----------
22H5	VH2|226	JH6	----------
16H7=23F8	VH2|226	JH6	----------N
24H11	VH2|226	JH6	----------
46D11	VH2|226	JH6	-----A----------
	Germline	Germline	FR1
			EVQLVESGGGLVKPGGSLRLSCAASGF TFS
18B11	VH3|315	JH6	----------
37D3	VH3|315	JH6	--H-------A----------R
	Germline	Germline	FR1
			EVQLLESGGGLVQPGGSLRLSCAASGF TFS
18G1	VH3|323	JH4	----------R----
12C11	VH3|323	JH4	----------R----
12E4	VH3|323	JH4	----------R----
17D8	VH3|323	JH4	----------Y----------
26H11	VH3|323	JH4	----------Y----------
	Germline	Germline	FR1
			QVQLVESGGGVVQPGRSLRLSCAASGF TFS
39F11=41H5=37G 3=39G8	VH3|333	JH6	----------
39F7=47E3=38F2	VH3|333	JH6	----------
39G5	VH3|333	JH6	----------V------
	Germline	Germline	FR1
			QVQLQESGPGLVKPSQTLSLTCTVSGG SIS
40D2=36F2=39C2	VH4|431	JH5	----------

	Germline	Germline	FR1
			QVQLQESGPGLVKPSETLSLTCTVSGGS IS
21B4	VH4|459	JH6	----------
21H2	VH4|459	JH6	----------

FIG. 13C

CDR1	FR2	CDR2
RASQGIRNDLG	WYQQKPGKAPKRLIY	AASSLQS
----D--Y---	----------	-------
CDR1	**FR2**	**CDR2**
RASQGISSWLA	WYQQKPGKAPKLLIY	AASSLQS
-------I---	----------	-------
CDR1	**FR2**	**CDR2**
KSSQSLLHSDGKTYLY	WYLQKPGQSPQLLIY	EVSSRFS
--------Q--------	---------P-H----	---N---
CDR1	**FR2**	**CDR2**
RSSQSLLHSNGYNYLD	WYLQKPGQSPQLLIY	LGSNRAS
----------F--	----------	---D---
CDR1	**FR2**	**CDR2**
RSSQSLLHSNGYNYLD	WYLQKPGQSPQLLIY	LGSNRAS
-------YY--FT---	-F-------H----	------
CDR1	**FR2**	**CDR2**
RASQSVSSSYLA	WYQQKPGQAPRLLIY	GASSRAT
----NFD--S--	----------	------
----NFD-----	----------	-T-----
--------GN---	----------	-------
--------T---	-H------GL-----	-------
--------T---	-H------GL-----	-------
--------GN---	----------	-------
----NFD-N---	----------	-------
--------T---	----------	-------
--------T---	---------S----	------
--------T---	----------	---F---
CDR1	**FR2**	**CDR2**
RASQSVSSNLA	WYQQKPGQAPRLLIY	GASTRAT
-------N----	----------	-V------
CDR1	**FR2**	**CDR2**
GGNNIGSKSVH	WYQQKPGQAPVLVIY	YDSDRPS
-------E---	----------V-	D------
-------E---	----------V-	D------
-------Q---	----------V-	D------
-------Q---	----------V-	D------

FIG. 13D

CDR1	FR2	CDR2
ELSMH	WVRQAPGKGLEWMG	GFDPEDGETIYAQKFQG
D----	----------	----------
CDR1	**FR2**	**CDR2**
NARMGVS	WIRQPPGKALEWLA	HIFSNDEKSYSTSLKS
-------	----------	----------
-------	----------	----------
-------	----------	----------
-------	----------	----------N
------N	----------	----------
CDR1	**FR2**	**CDR2**
NAWMS	WVRQAPGKGLEWVG	RIKSKTDGGTTDYAAPVKG
D----	----------	----------
-----	----------	----------
CDR1	**FR2**	**CDR2**
SYAMS	WVRQAPGKGLEWVS	AISGSGGSTYYADSVKG
T----	----------	G-----V--H-------
T----	----------	G----V----------
T----	----------	G-----V----------
T----	----------	------V----------
T----	----------	------V--N------
CDR1	**FR2**	**CDR2**
SYGMH	WVRQAPGKGLEWVA	VIWYDGSNKYYADSVKG
---I-	----------	-------D---------
N--I-	----------	------I----------
---I-	----------	------D--G------
CDR1	**FR2**	**CDR2**
SGGYYWS	WIRQHPGKGLEWIG	YIYYSGSTYYNPSLKS
----N--	----------	N----------

CDR1	FR2	CDR2
SYYWS	WIRQPPGKGLEWIG	YIYYSGSTNYNPSLKS
---F--	------A--------	R--T----------
-----	------A--------	R--T----------

FIG. 13E

FR3	CDR3	FR4
GVPSRFSGSGSGTEFTLTISSLQPEDFATYYC		
----------V----------	LQHNSYPLT	FGGGTKVEIE
FR3	**CDR3**	**FR4**
GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC		
----------	QQANDFPIT	FGQGTRLEIK
FR3	**CDR3**	**FR4**
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC		
----------	MQSIQLPRT	FGQGTKVEIK
FR3	**CDR3**	**FR4**
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC		
----------E----------L---	MQALQTPCS	FGQGTKLEIK
FR3	**CDR3**	**FR4**
GVPDRFSGSGSGTDFTLKISRVEAEDVGVYYC		
--------V----------	MQSLQTPFT	FGPGTKVDIK
FR3	**CDR3**	**FR4**
GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC		
----------M---	QQCGSSPLT	FGGGTKVEIK
-------I---------N-------M---	QQYGGSPLT	FGGGTEVEIK
----------	QQYGSAPLT	FGGGTKVEIK
----------	QQYGSSFT	FGGGTRVEIK
----------	QQYGSSFT	FGGGTRVEIK
----------M---	QQYGSSPLT	FGGGSKVEIK
----N----------M---	QQYGSSPLT	FGGGTKVEIK
----------	QQSGSSPLT	FGGGTEVEIK
----------	QQSGSSPLT	FGGGTKVEIK
----------	QQSGSSPLT	FGGGTKVEIK
FR3	**CDR3**	**FR4**
GIPARFSGSGSGTEFTLTISSLQSEDFAVYYC		
----------R----------	QQYNNWPPT	FGQGTKVEIK
FR3	**CDR3**	**FR4**
GIPERFSGSNSGNTATLTISRVEAGDEADYYC		
----------	QVWDGNSDHVV	FGGGTKLTVL
----------	QVWDGNSDHVV	FGGGTKLTVL
----------	QVWDNTSDHVV	FGGGTKLTVL
----------	QVWDSSSDHVV	FGGGTKLTVL

FIG. 13F

FR3	CDR3	FR4
RVTMTEDTSTDTAYMELSSLRS EDTAVYYCAT		
-|----------S	IVVVPAAIQSYYYYYGMGV	WGQGTTVTVSS
FR3	**CDR3**	**FR4**
RLTISKDTSKSQVVLTMTNMDPV DTATYYCAR		
----------	ILLLGAYYYYGMDV	WGQGTTVTVSS
----------	ILLVGAYYYCGMDV	WGQGTTVTVSS
----------|----------	SVVTGGYYYDGMDV	WGQGTTVTVSS
----------|----------	SVVTGGYYYDGMDV	WGQGTTVTVSS
----------	VRIAGDYYYYYGMDV	WGQGTTVTVSS
FR3	**CDR3**	**FR4**
RFTISRDDSKNTLYLQMNSLKTE DTAVYYCTT		
----------F--S	TYSSGWYVWDYYGMDV	WGQGTTVTVSS
----------E--|-	DRVLSYYAMAV	WGQGTTVTVSS
FR3	**CDR3**	**FR4**
RFTISRDNSKNTLYLQMNSLRAE DTAVYYCAK		
----------	SLIVVIVYALDH	WGQGTLVTVSS
----------	SLIVVIVYALDY	WGQGTLVTVSS
----------	SLIVVIVYALDY	WGQGTLVTVSS
----------	SLIVVMVYVLDY	WGQGTLVTVSS
----------	SLIVVMVYVLDY	WGQGTLVTVSS
FR3	**CDR3**	**FR4**
RFTISRDNSKNTLYLQMNSLRAE DTAVYYCAR		
----------	DRAAAGLHYYYGMDV	WGQGTTVTVSS
----------	DRAAAGLHYYYGMDV	WGQGTTVTVSS
----------	DRAAAGLHYYYGMDV	WGQGTTVTVSS
FR3	**CDR3**	**FR4**
RVTISVDTSKNQFSLKLSSVTAA DTAVYYCAR		
----------R----------	ENIVVIPAAIFAGWFDP	WGQGTLVTVSS

FR3	CDR3	FR4
RVTISVDTSKNQFSLKLSSVTAA DTAVYYCAR		
---M-|----------	DPDGDYYYYGMDV	WGQGTTVTVSS
---M-K----------R----------	DPDGDYYYYGMDV	WGQGTSVTVSS

FIG. 14

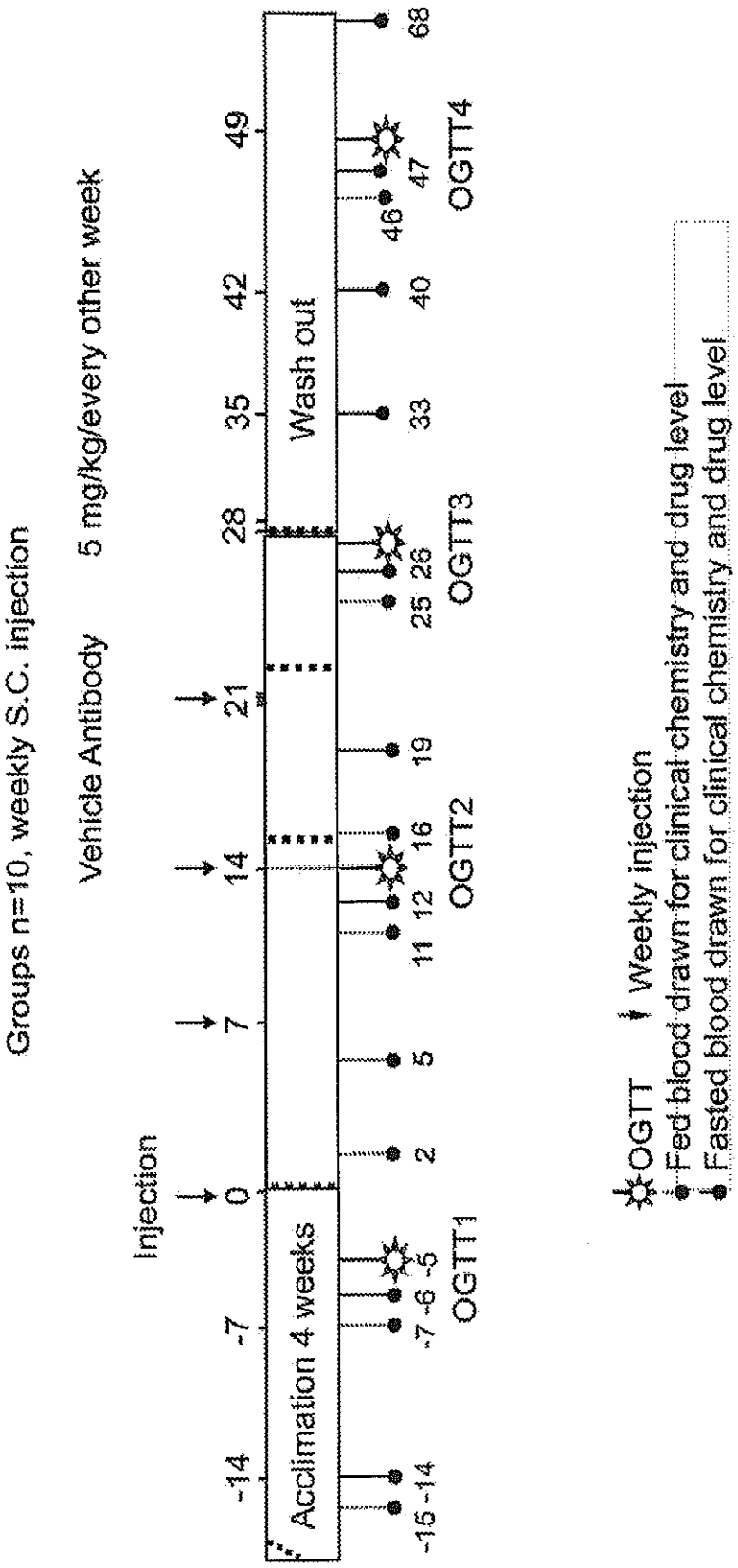

Groups n=10, weekly S.C. injection
Vehicle Antibody 5 mg/kg/every other week
Injection
Acclimation 4 weeks
Wash out
OGTT1
OGTT2
OGTT3
OGTT4
-14
-7
0
7
14
21
28
35
42
49
68
-15 -14
-7 -6 -5
2
5
11 12
16
19
25 26
33
40
46
47
OGTT
Weekly injection
Fed blood drawn for clinical chemistry and drug level
Fasted blood drawn for clinical chemistry and drug level

FIG. 15

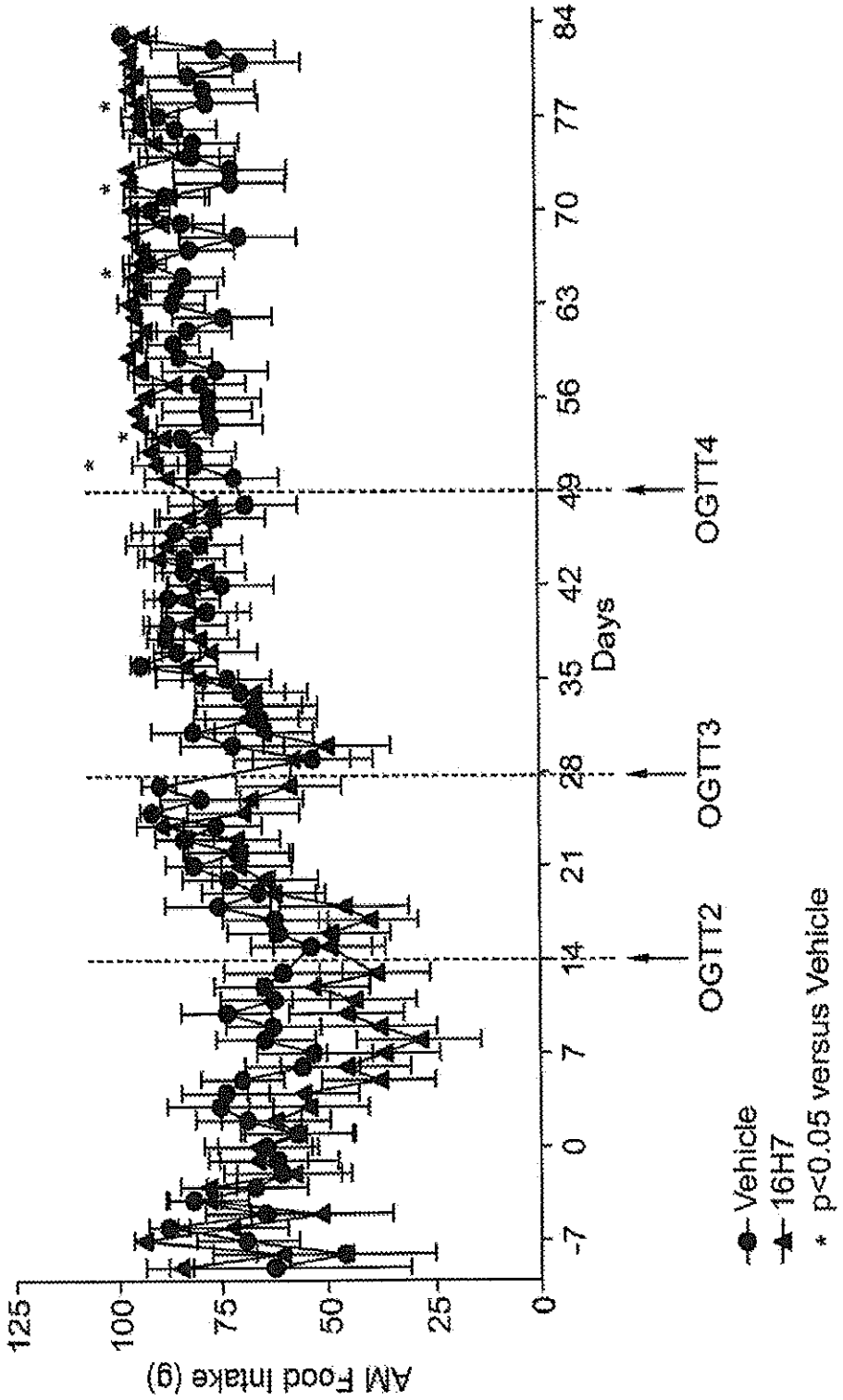

AM Food Intake (g)
125
100
75
50
25
0
-7
0
7
14
21
28
35
42
49
56
63
70
77
84
Days
OGTT2
OGTT3
OGTT4
Vehicle
16H7
* p<0.05 versus Vehicle

FIG. 16A

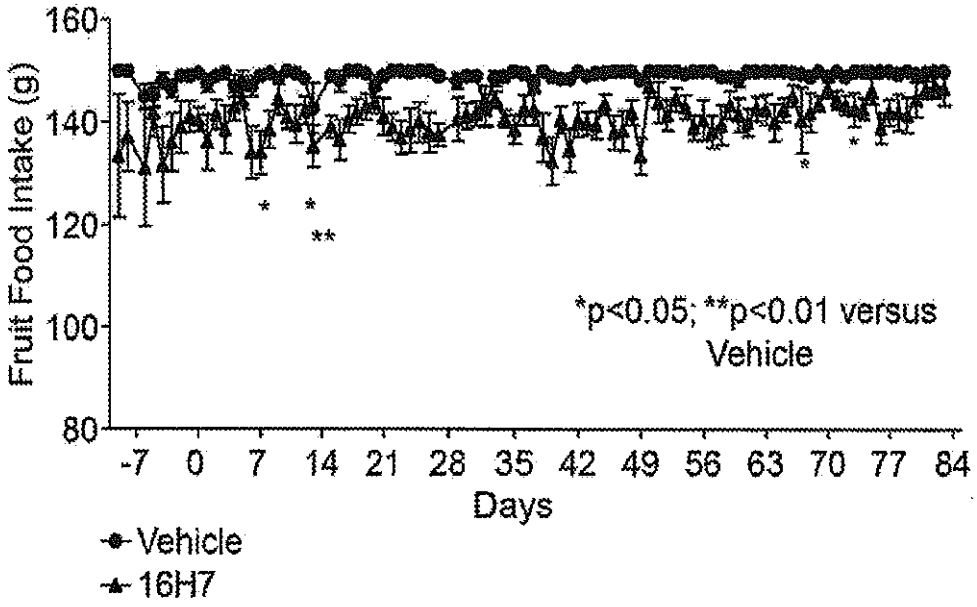


FIG. 16B

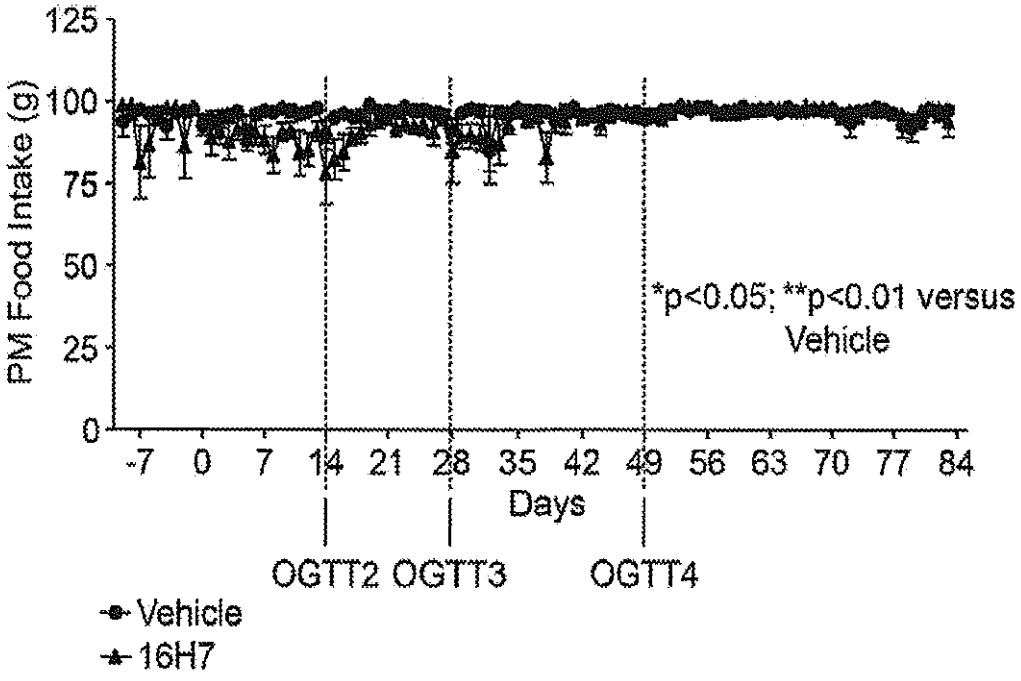
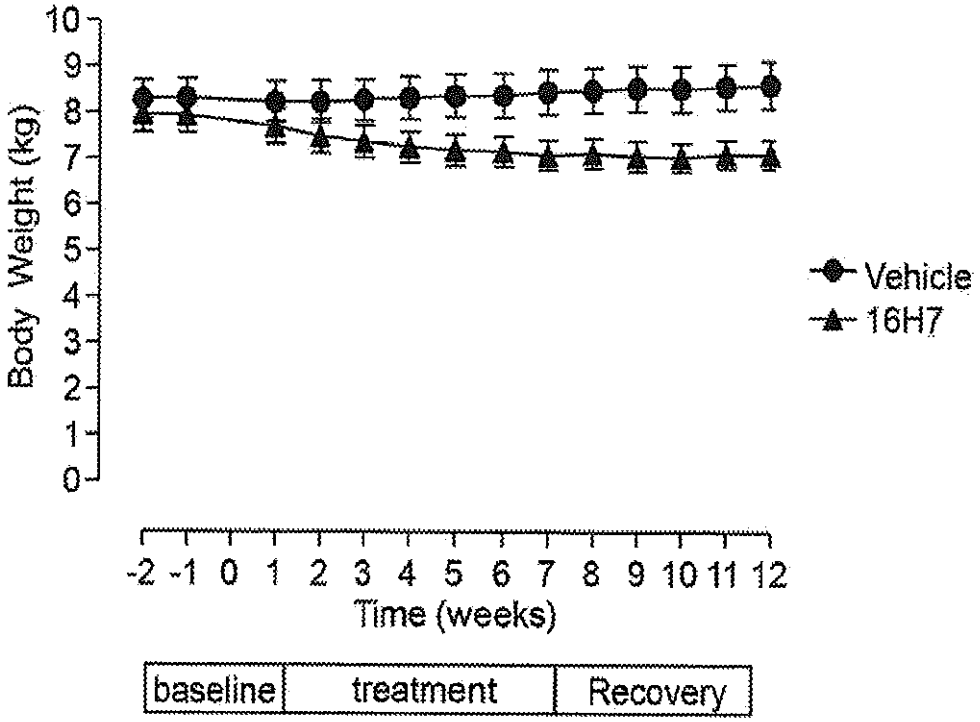
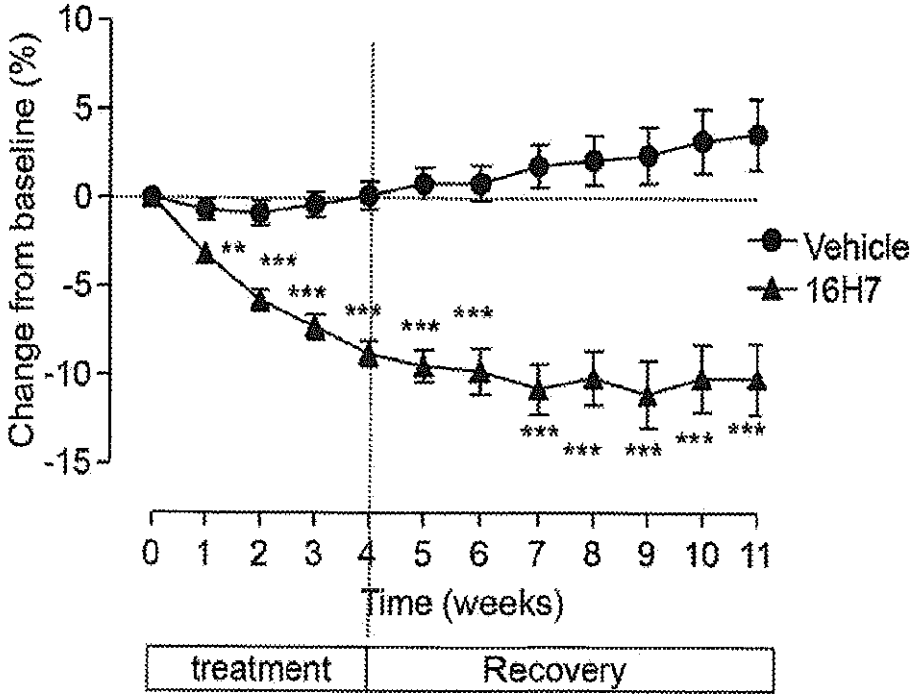


FIG. 17A



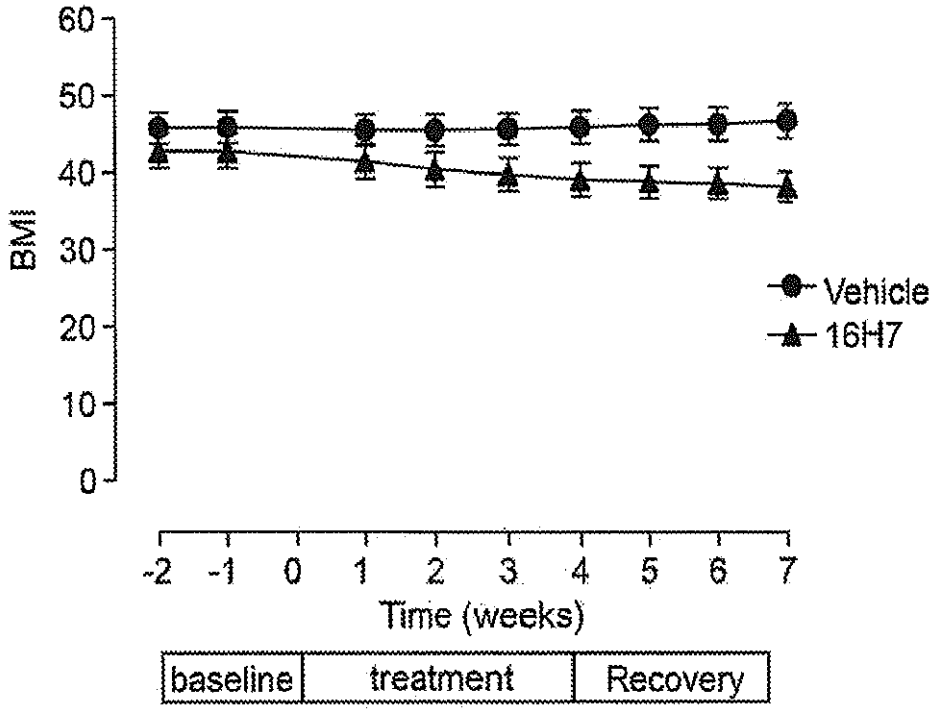
*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 17B



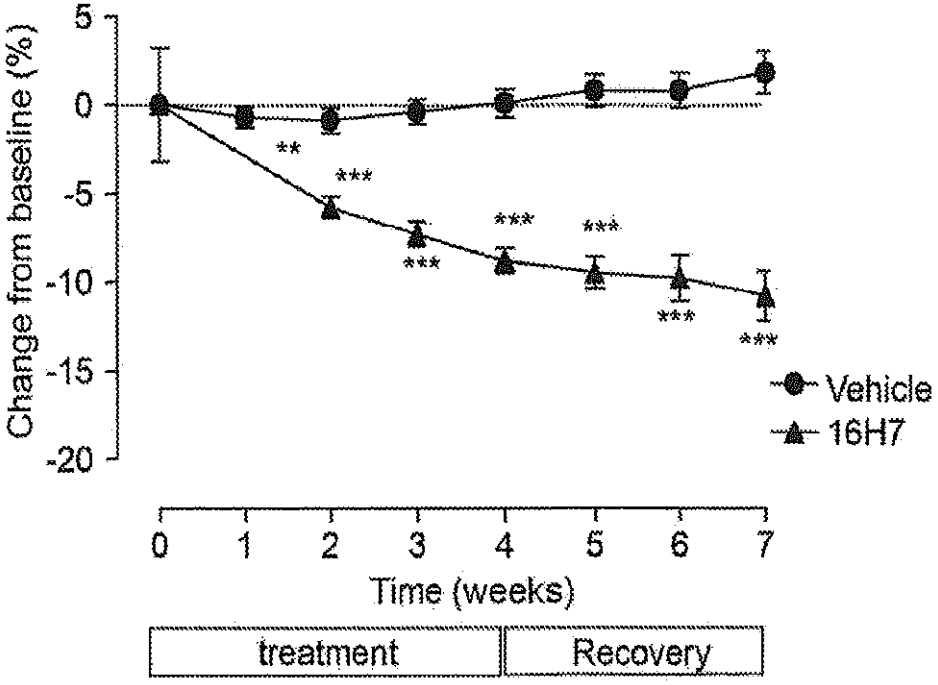
*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 18A



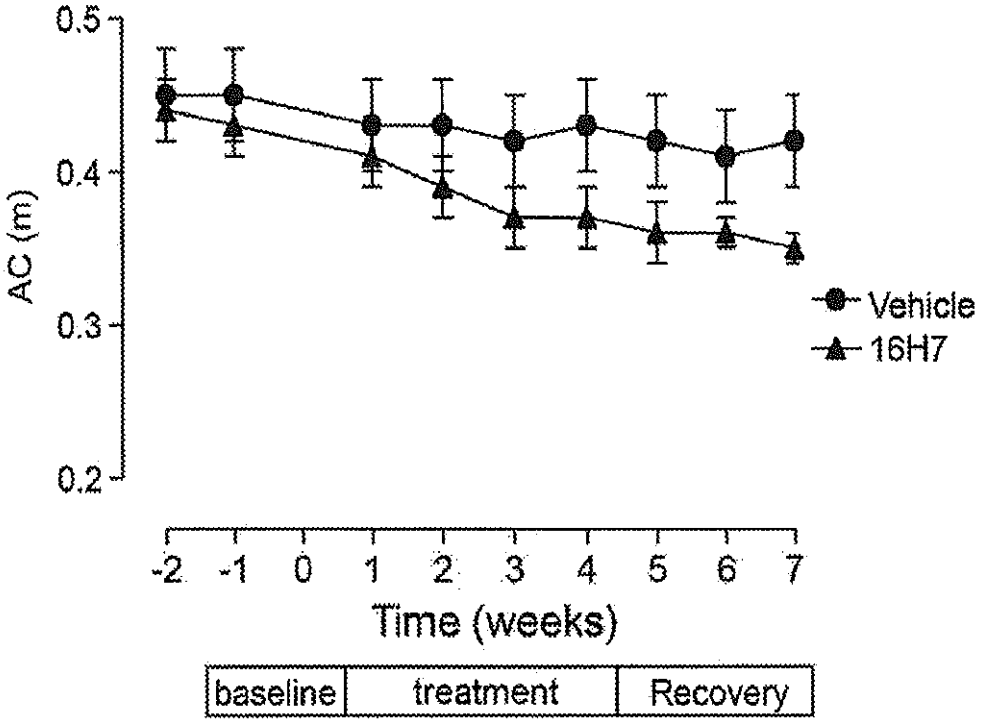
*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 18B



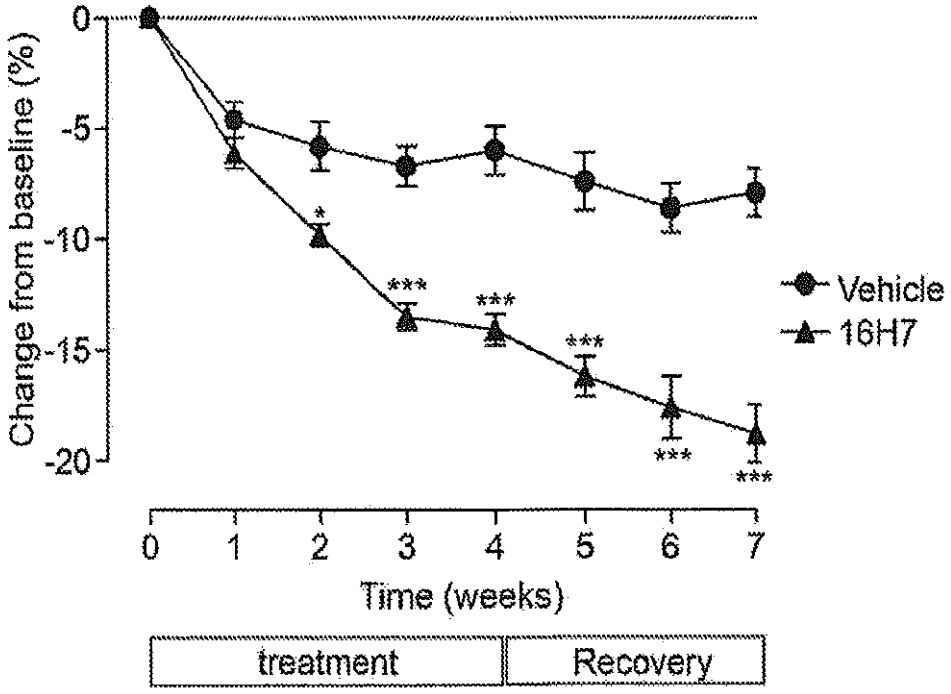
*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 19A



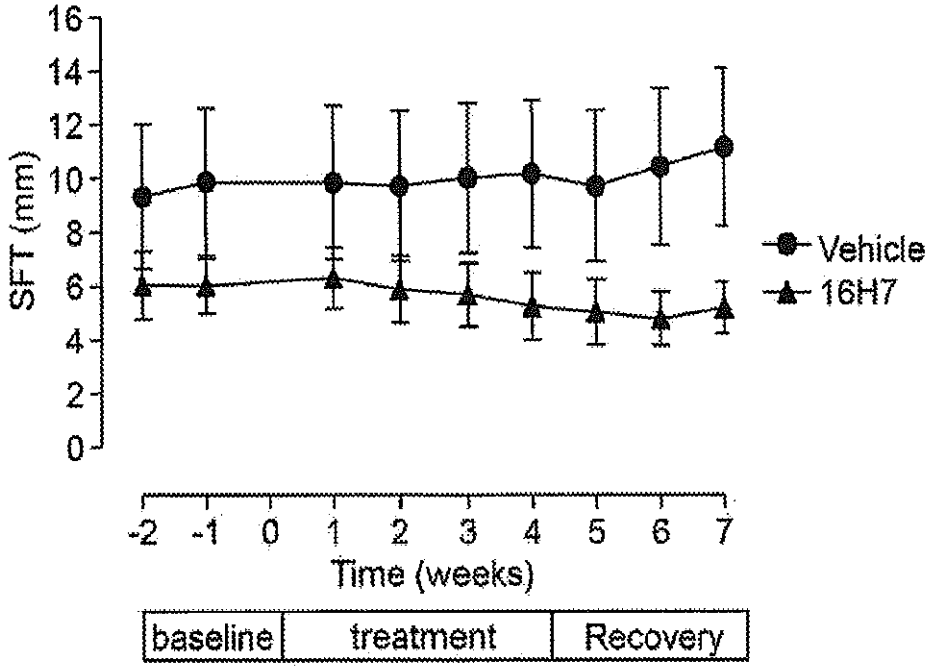
*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 19B



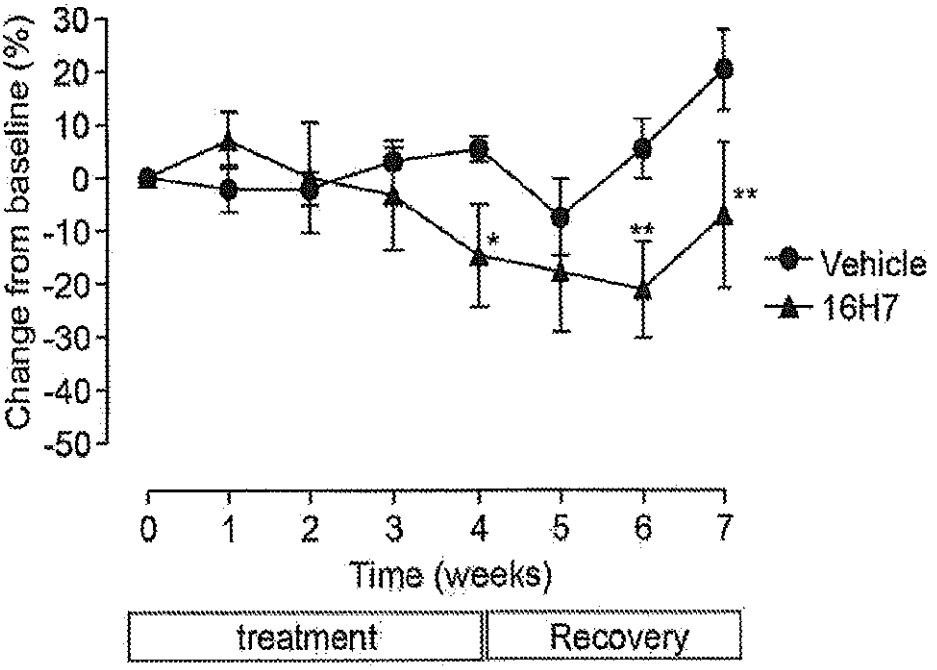
*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 20A



*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 20B



*p<0.05; **p<0.01***p<0.001 versus Vehicle

FIG. 21A

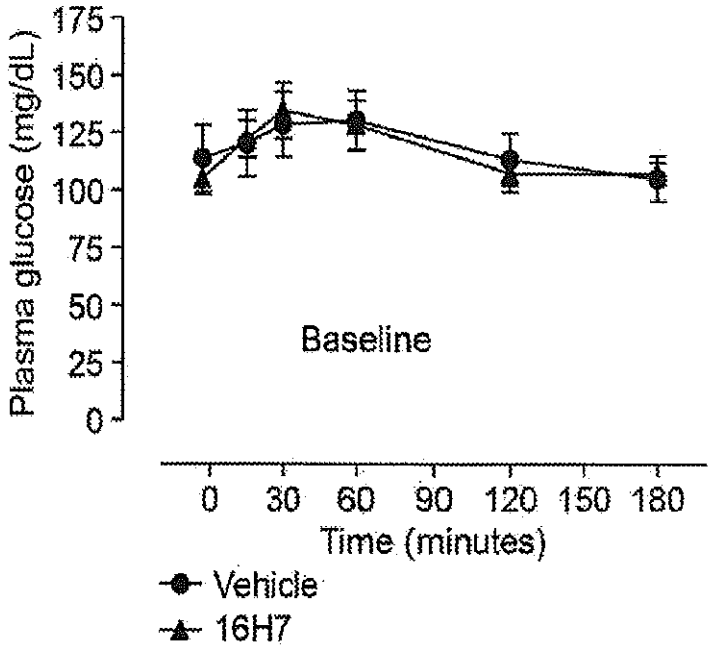


FIG. 21B

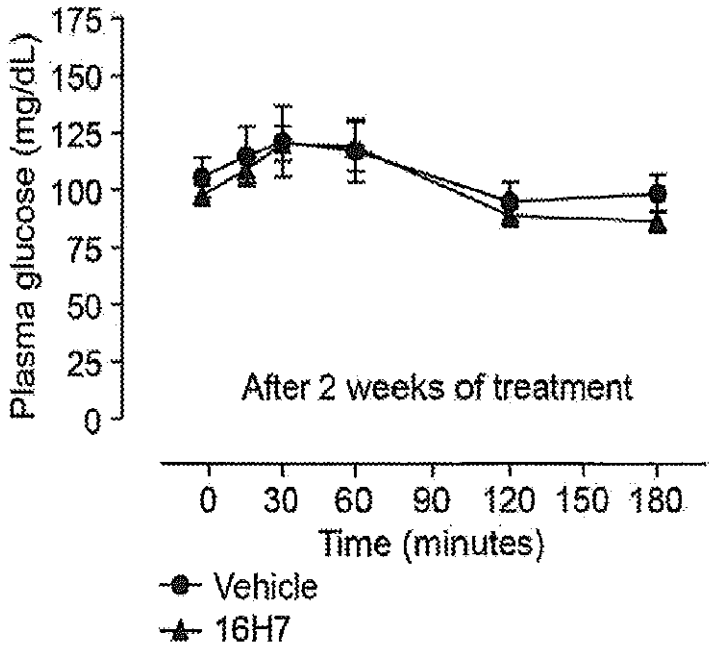


FIG. 21C

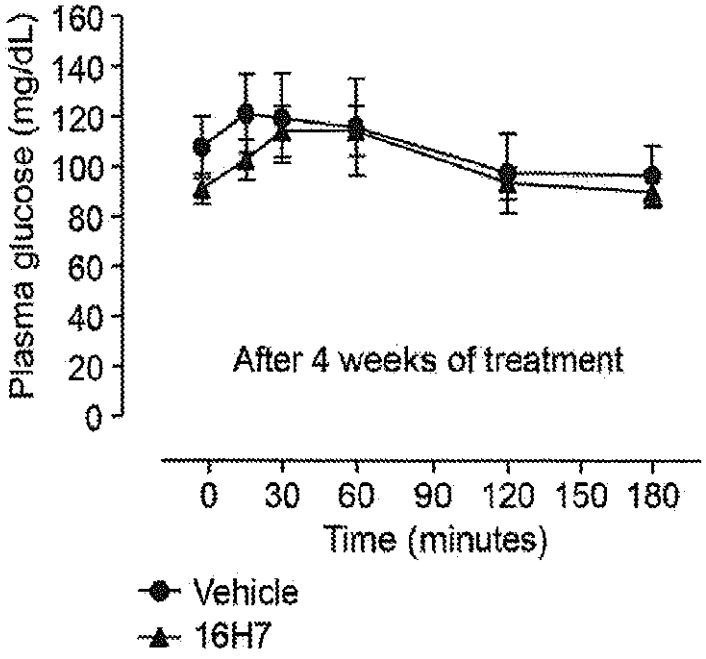


FIG. 21D

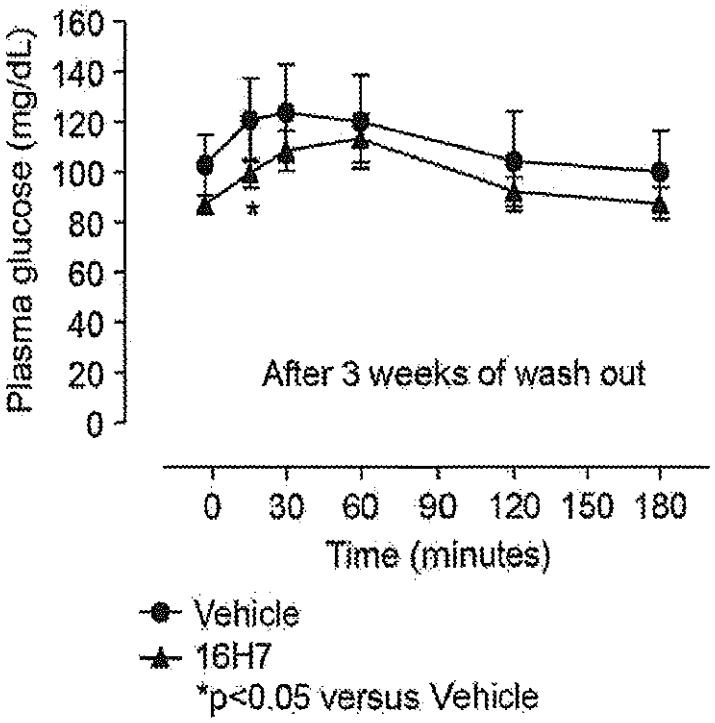


FIG. 22A

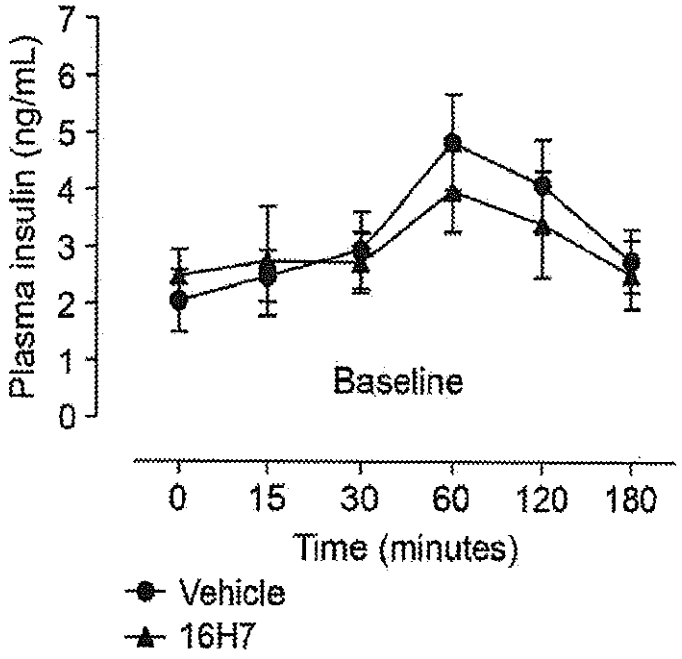


FIG. 22B

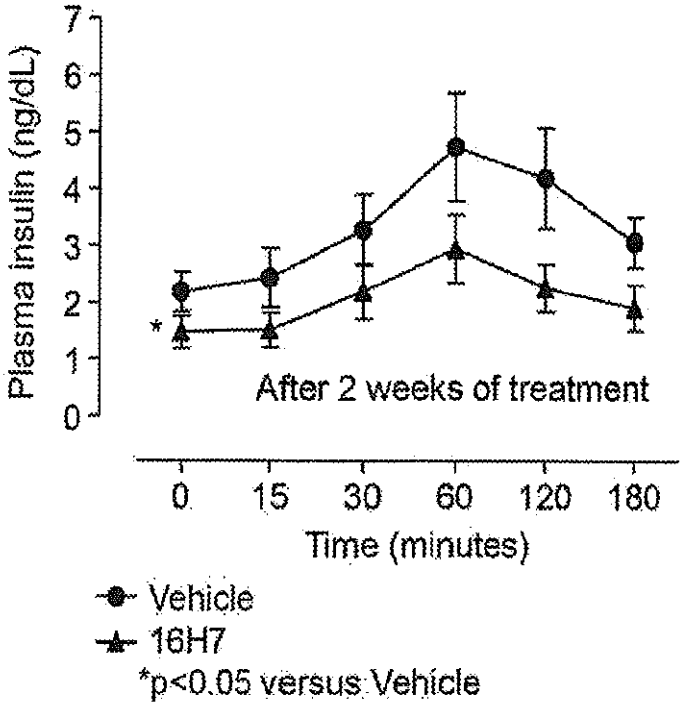


FIG. 22C

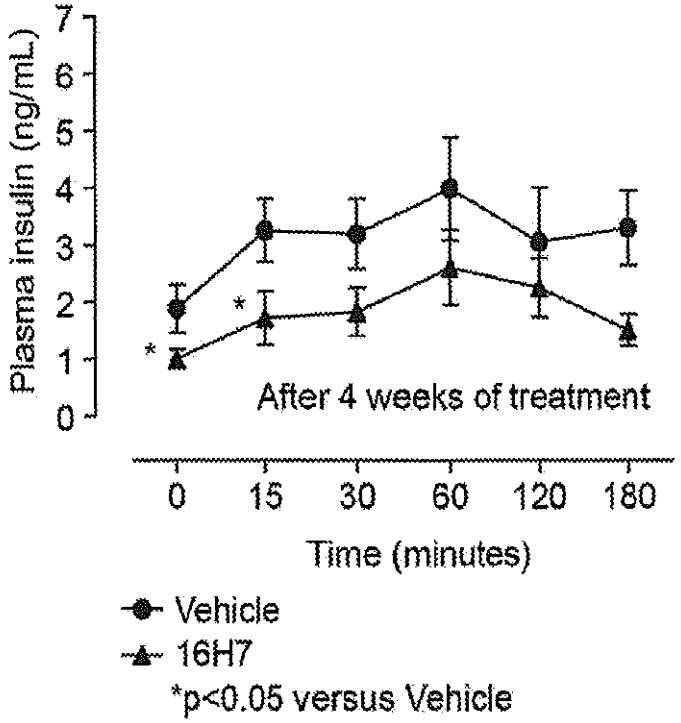


FIG. 22D

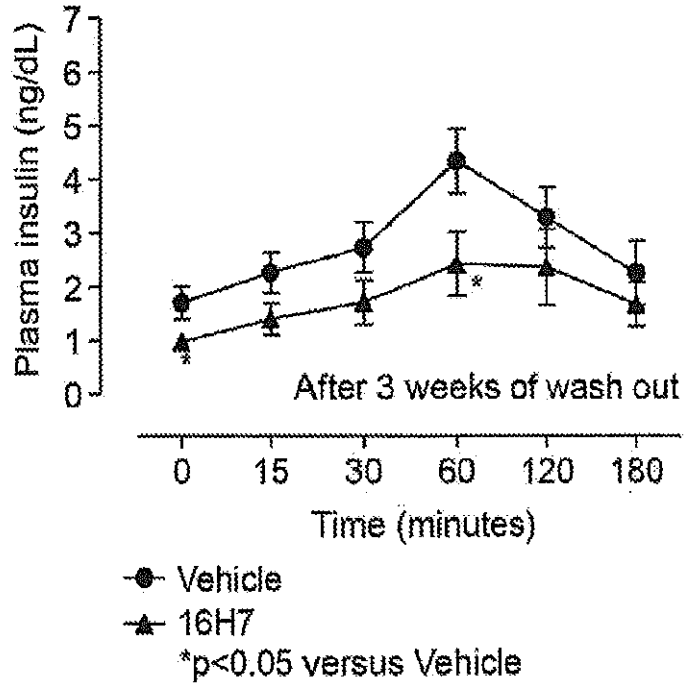


FIG. 23A

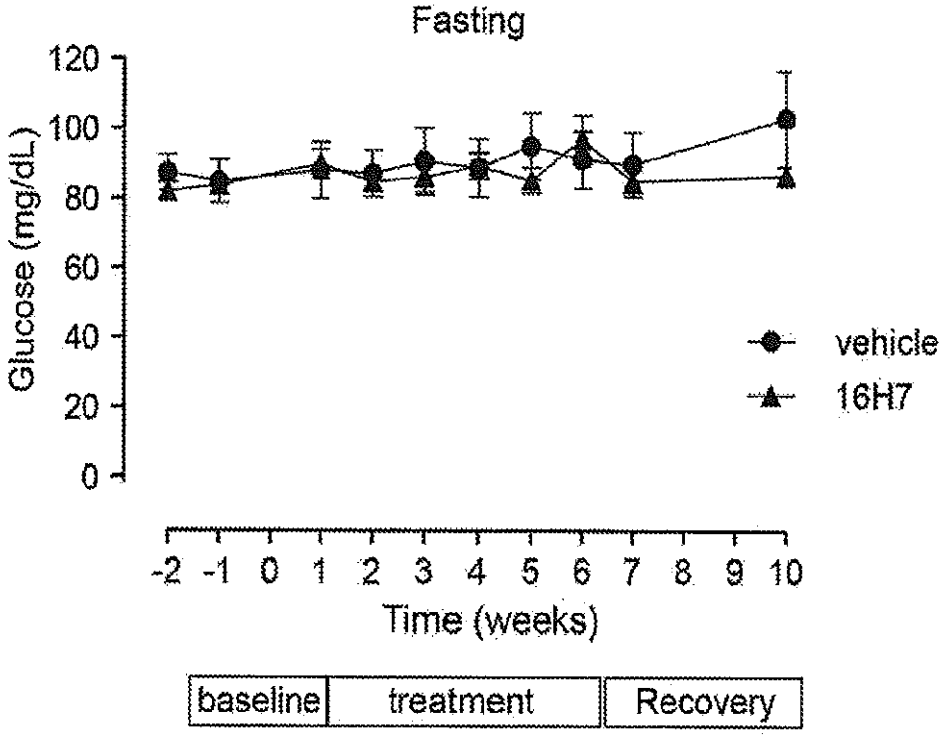


FIG. 23B

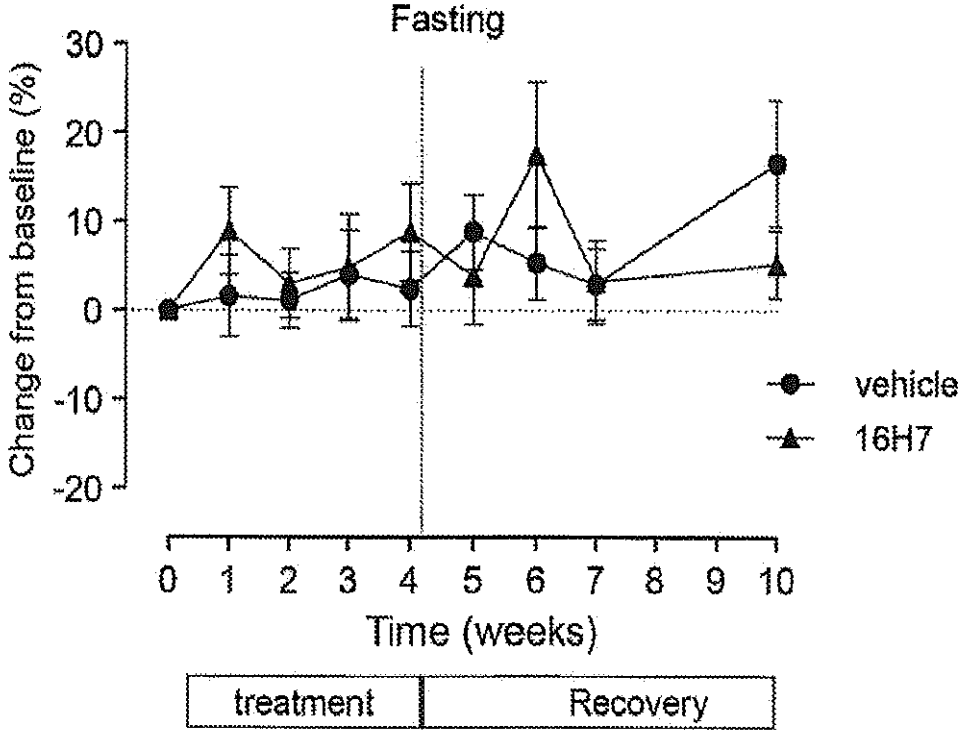


FIG. 24A

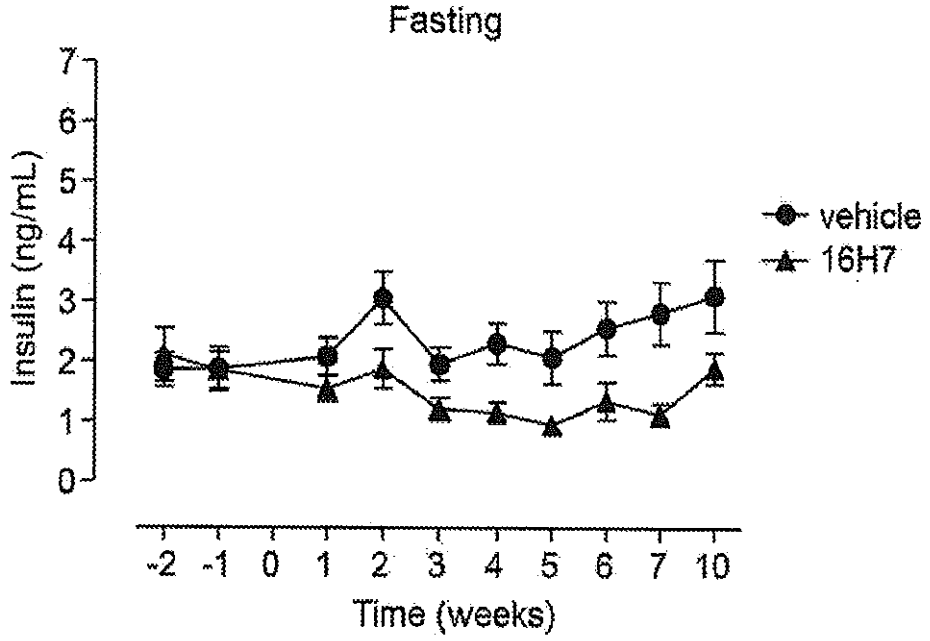
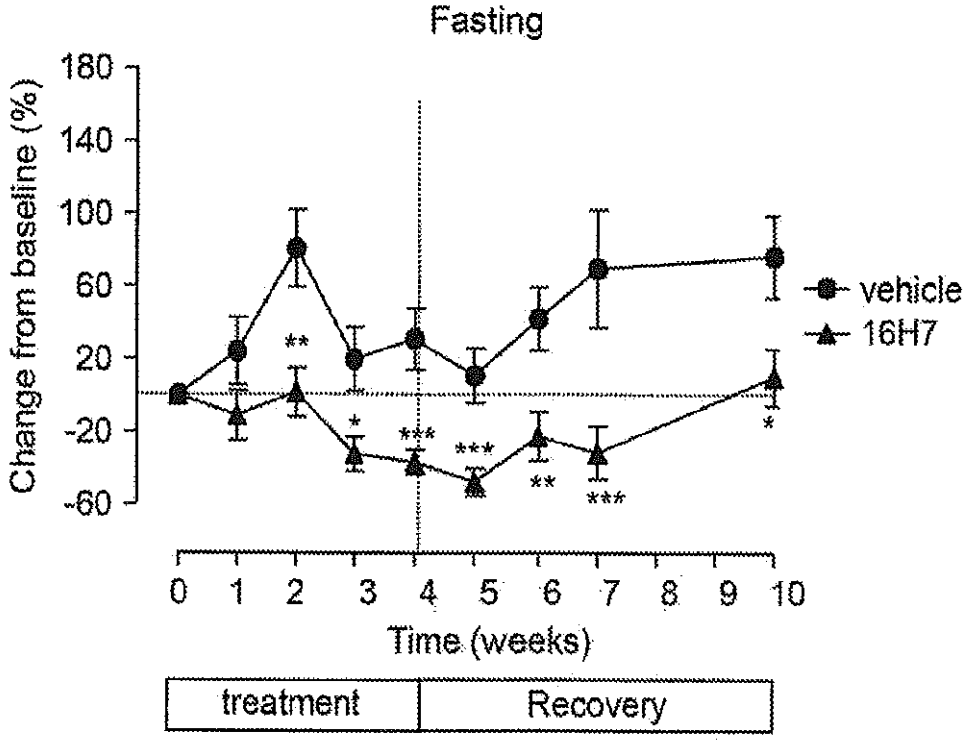
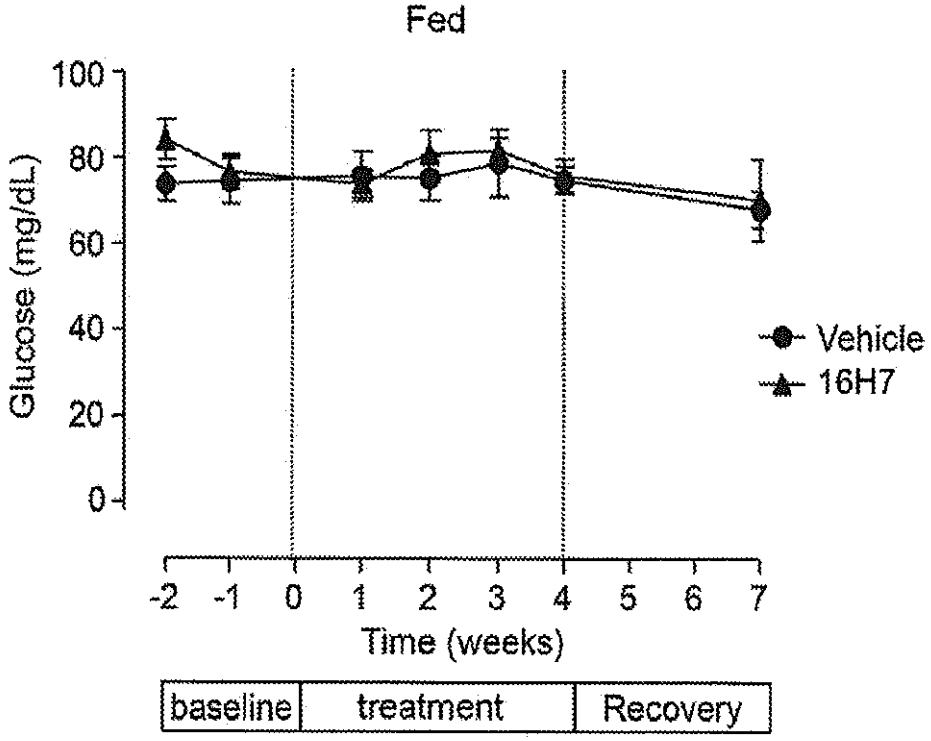


FIG. 24B



*p<0.05; **p<0.01; ***p<0.001 versus Vehicle

FIG. 25A



*p<0.05; **p<0.01; ***p<0.001 versus Vehicle

FIG. 25B

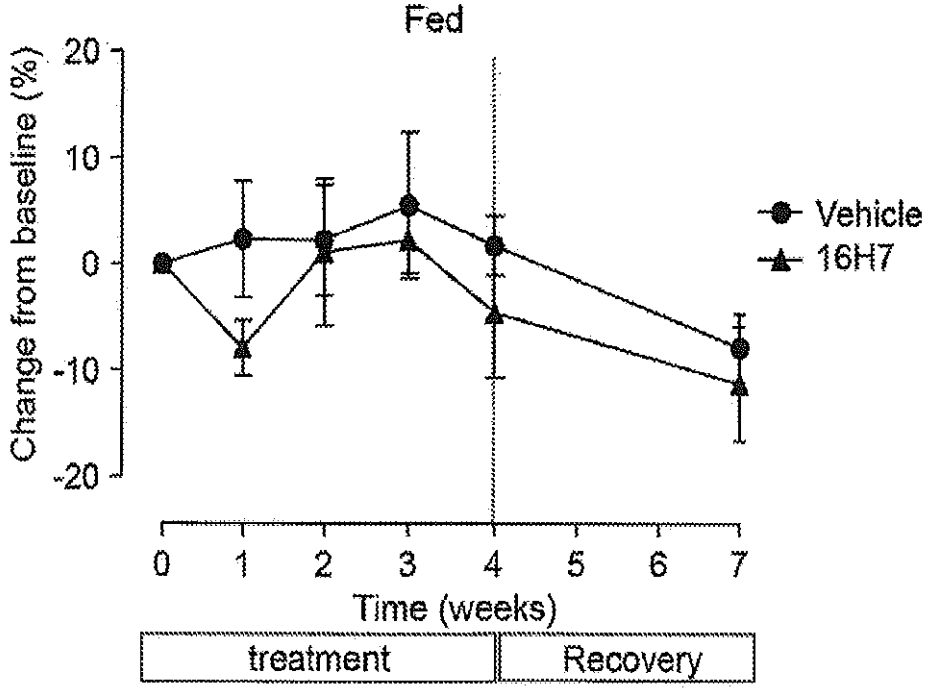
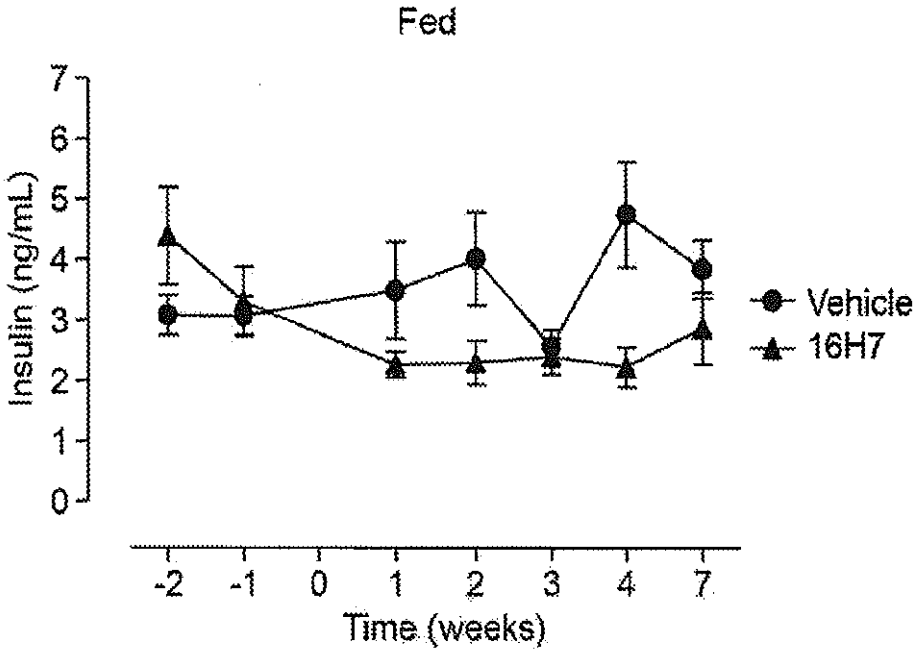


FIG. 26A



*p<0.05; **p<0.01; ***p<0.001 versus Vehicle

FIG. 26B

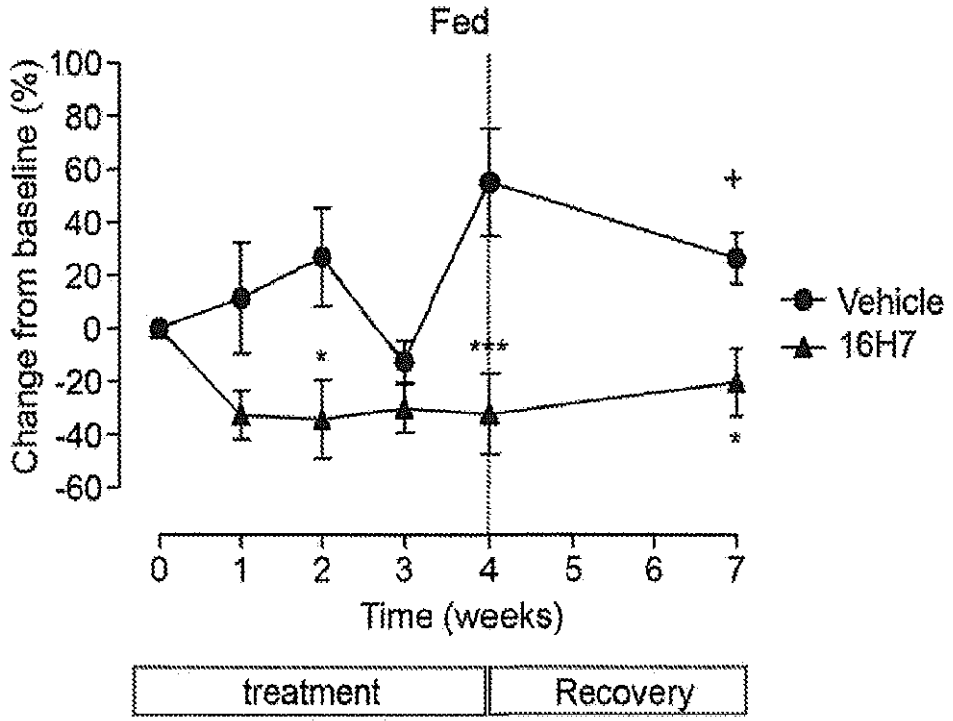
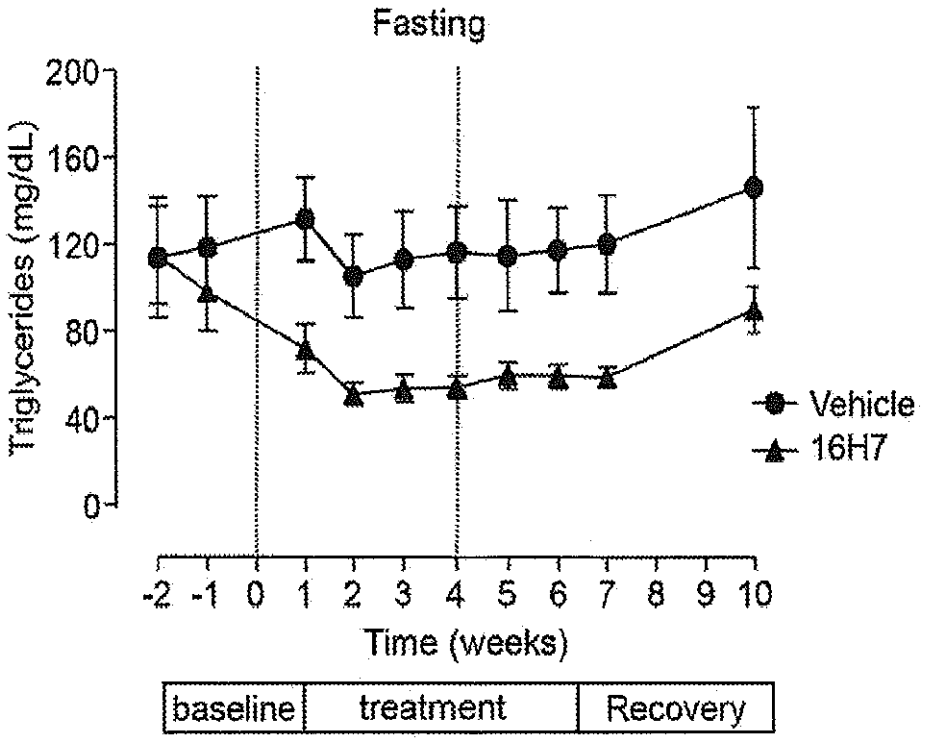


FIG. 27A



*p<0.05; **p<0.01; ***p<0.001 versus Vehicle

FIG. 27B

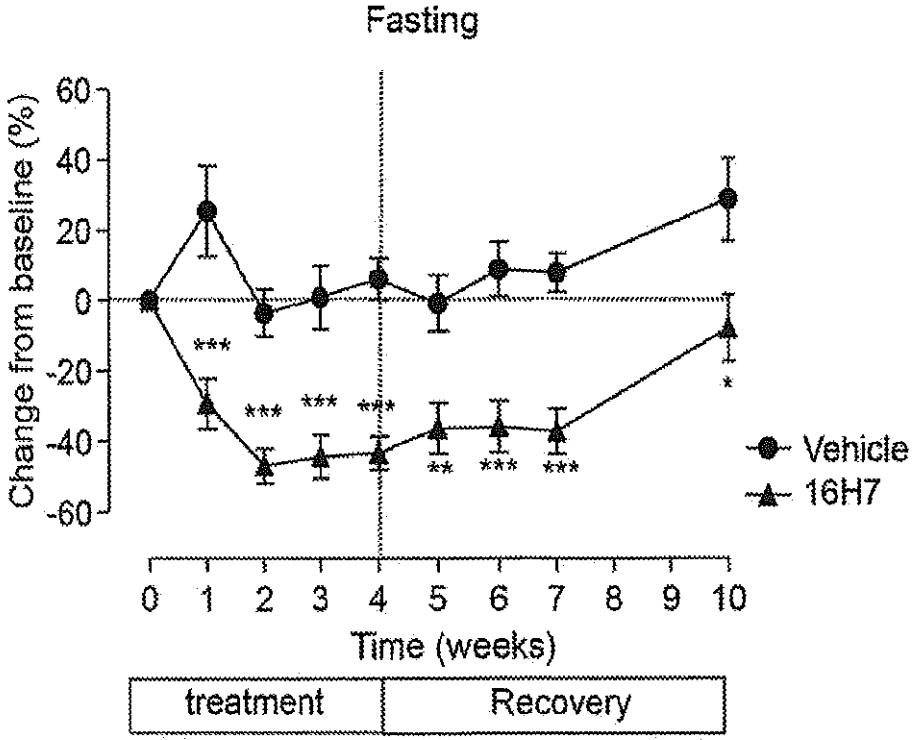
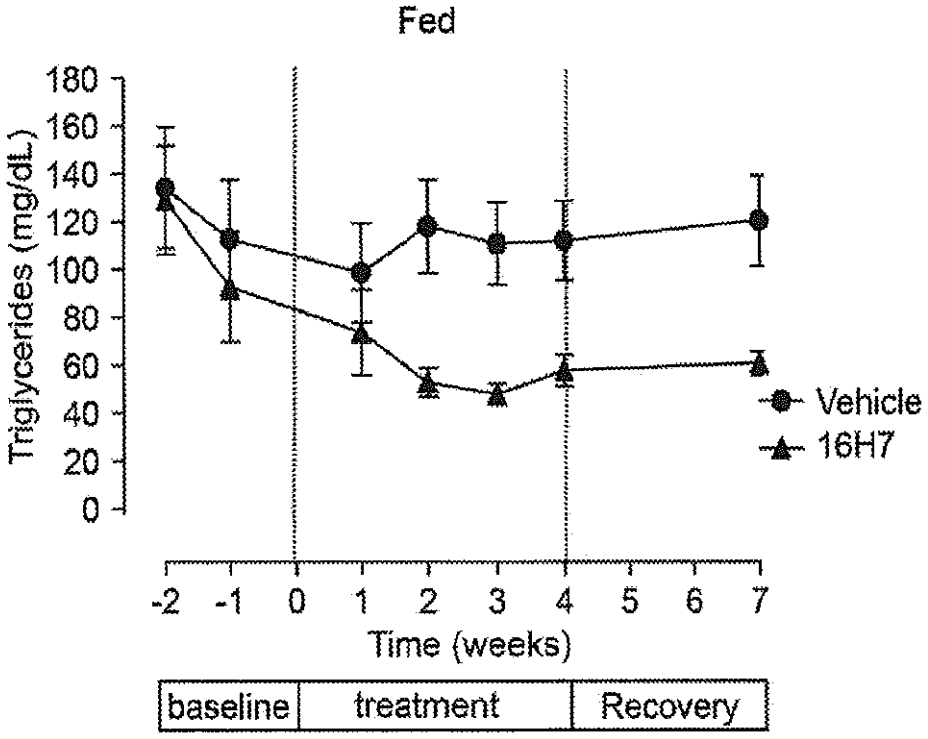


FIG. 28A



*p<0.05; **p<0.01; ***p<0.001 versus Vehicle

FIG. 28B

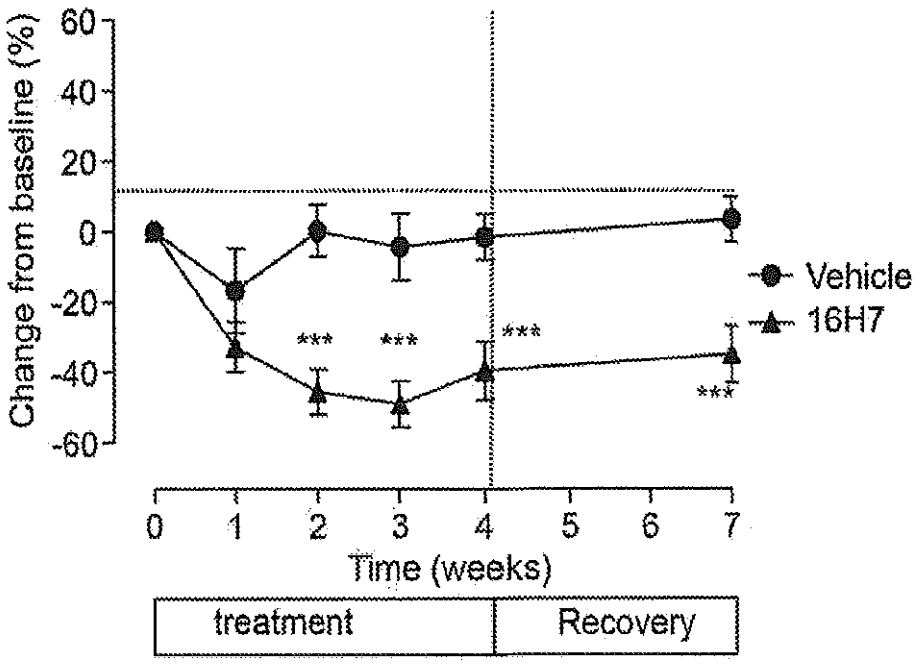
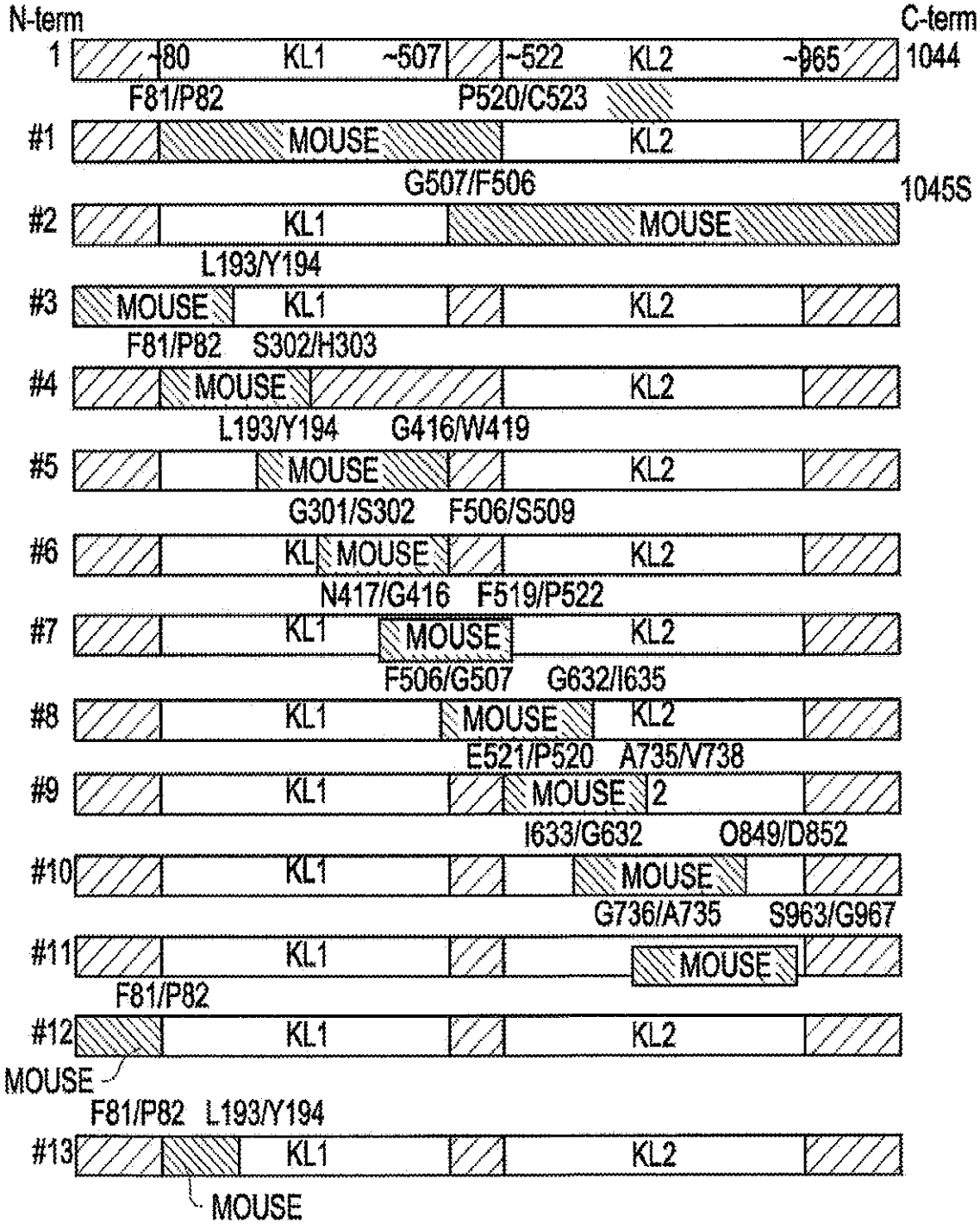


FIG. 29


N-term
C-term
1
~80
KL1
~507
~522
KL2
~965
1044
F81/P82
P520/C523
#1
MOUSE
KL2
G507/F506
1045S
#2
KL1
MOUSE
L193/Y194
#3
MOUSE
KL1
KL2
F81/P82
S302/H303
#4
MOUSE
KL2
L193/Y194
G416/W419
#5
MOUSE
KL2
G301/S302
F506/S509
#6
KL
MOUSE
KL2
N417/G416
F519/P522
#7
KL1
MOUSE
KL2
F506/G507
G632/I635
#8
KL1
MOUSE
KL2
E521/P520
A735/V738
#9
KL1
MOUSE
2
I633/G632
O849/D852
#10
KL1
MOUSE
G736/A735
S963/G967
#11
KL1
MOUSE
F81/P82
#12
KL1
KL2
MOUSE
F81/P82
L193/Y194
#13
KL1
KL2
MOUSE

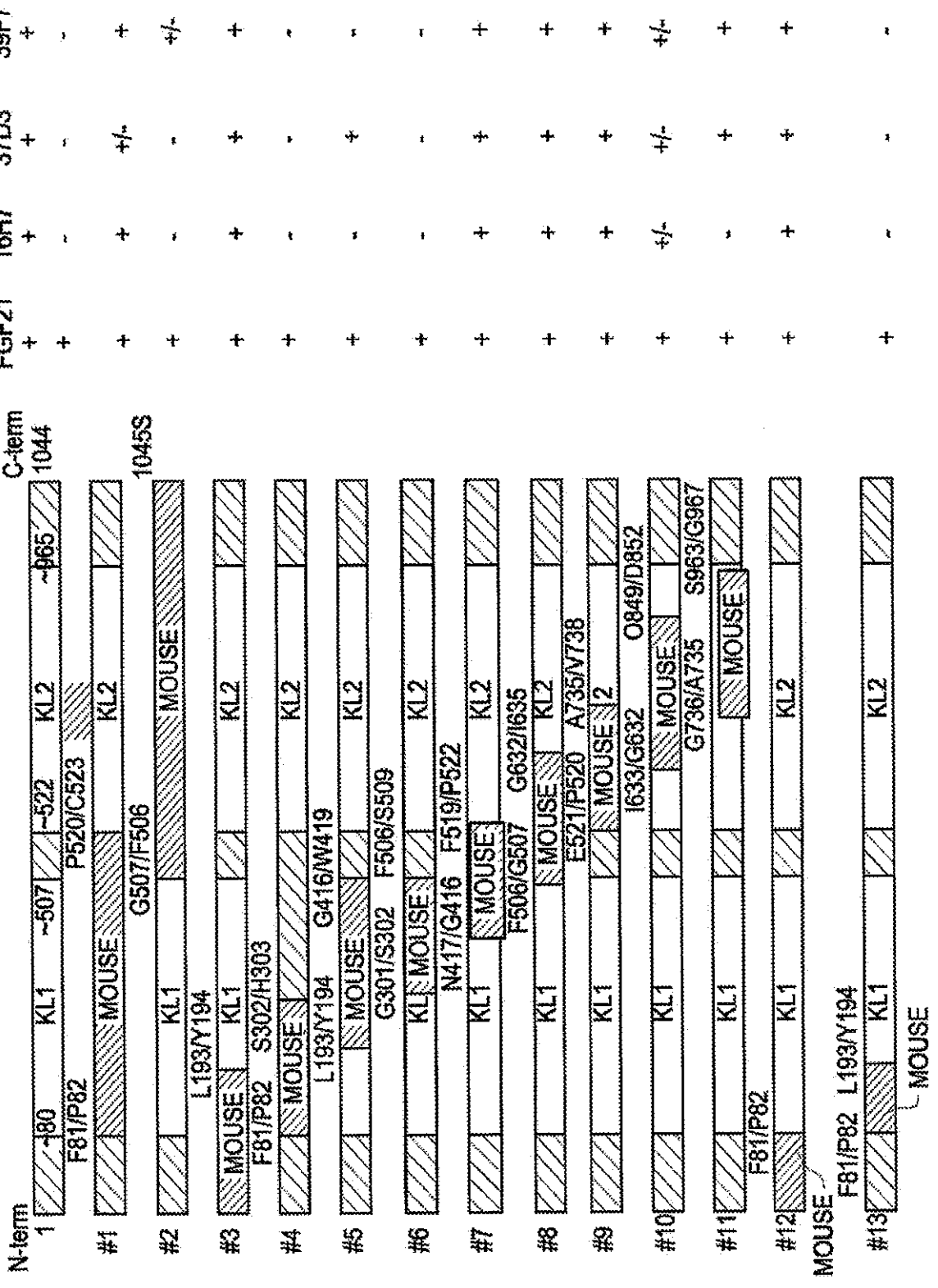

FGF21
16H7
37D3
39F7
N-term
1
~80
KL1
~507
~522
KL2
~965
C-term
1044
F81/P82
P520/C523
#1
MOUSE
G507/F506
1045S
#2
KL1
L193/Y194
#3
MOUSE
KL1
F81/P82
S302/H303
#4
MOUSE
L193/Y194
G416/W419
#5
MOUSE
G301/S302
F506/S509
#6
KL1
MOUSE
N417/G416
F519/P522
#7
KL1
MOUSE
F506/G507
G632/I635
#8
KL1
MOUSE
E521/P520
A735/V738
#9
KL1
MOUSE
I633/G632
O849/D852
#10
KL1
MOUSE
G736/A735
S963/G967
#11
KL1
MOUSE
F81/P82
#12
KL1
MOUSE
F81/P82
L193/Y194
#13
KL1
MOUSE

FIG. 30

FIG. 31A

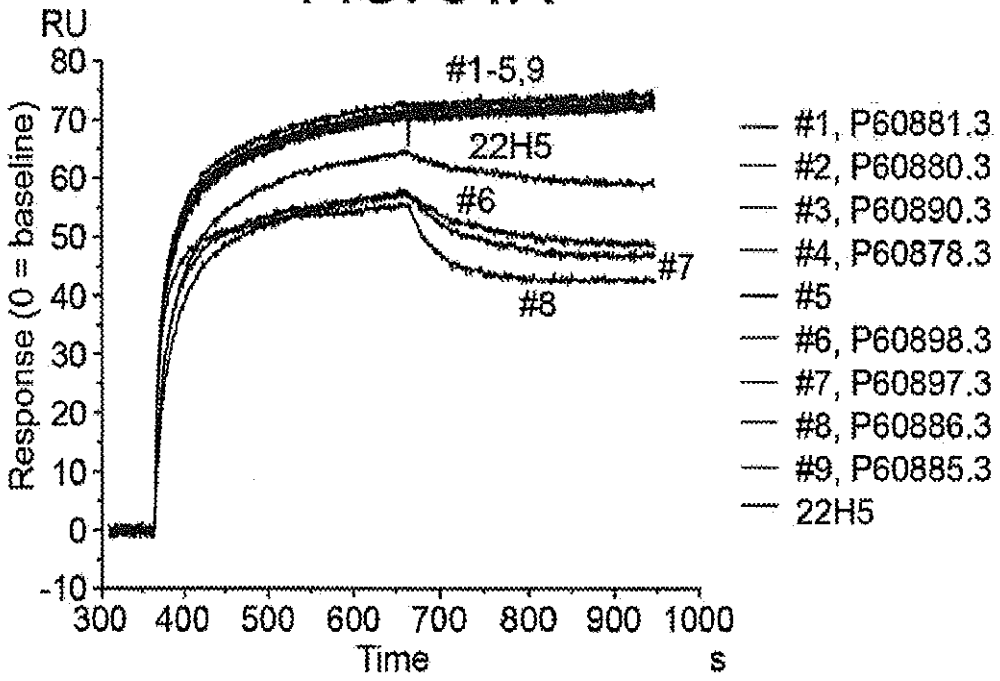


FIG. 31B

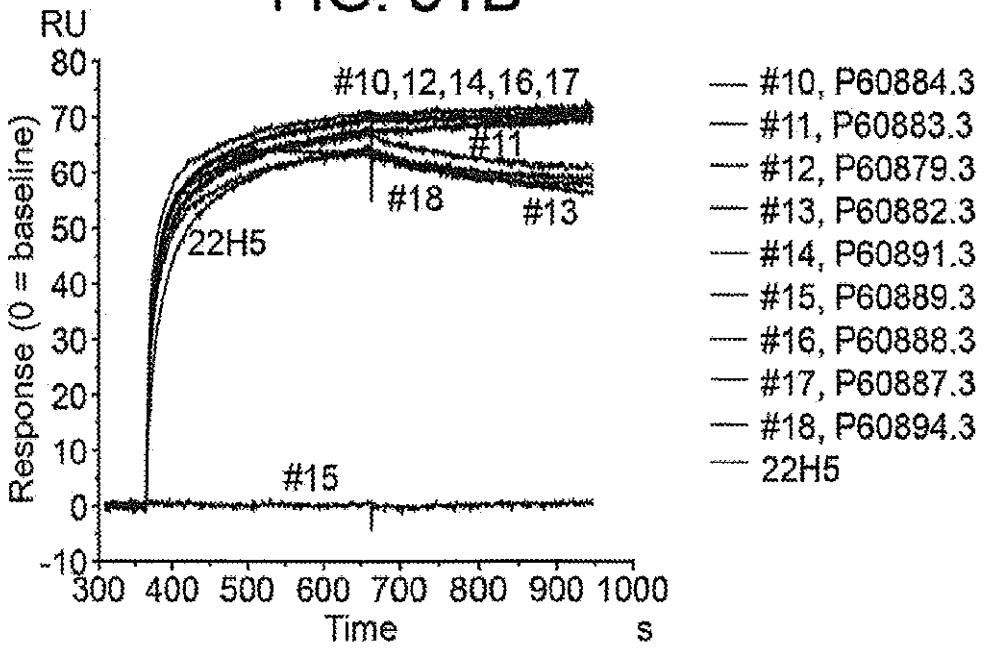


FIG. 31C

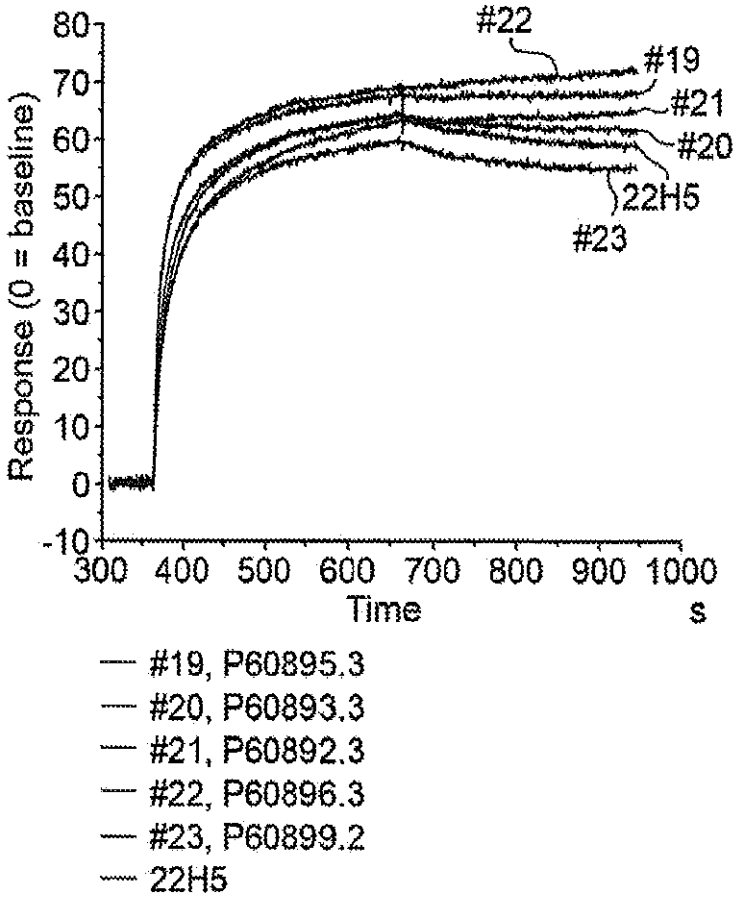

#22
#19
#21
#20
22H5
#23
Response (0 = baseline)
80
70
60
50
40
30
20
10
0
-10
300 400 500 600 700 800 900 1000
Time
s
#19, P60895.3
#20, P60893.3
#21, P60892.3
#22, P60896.3
#23, P60899.2
22H5

FIG. 32A

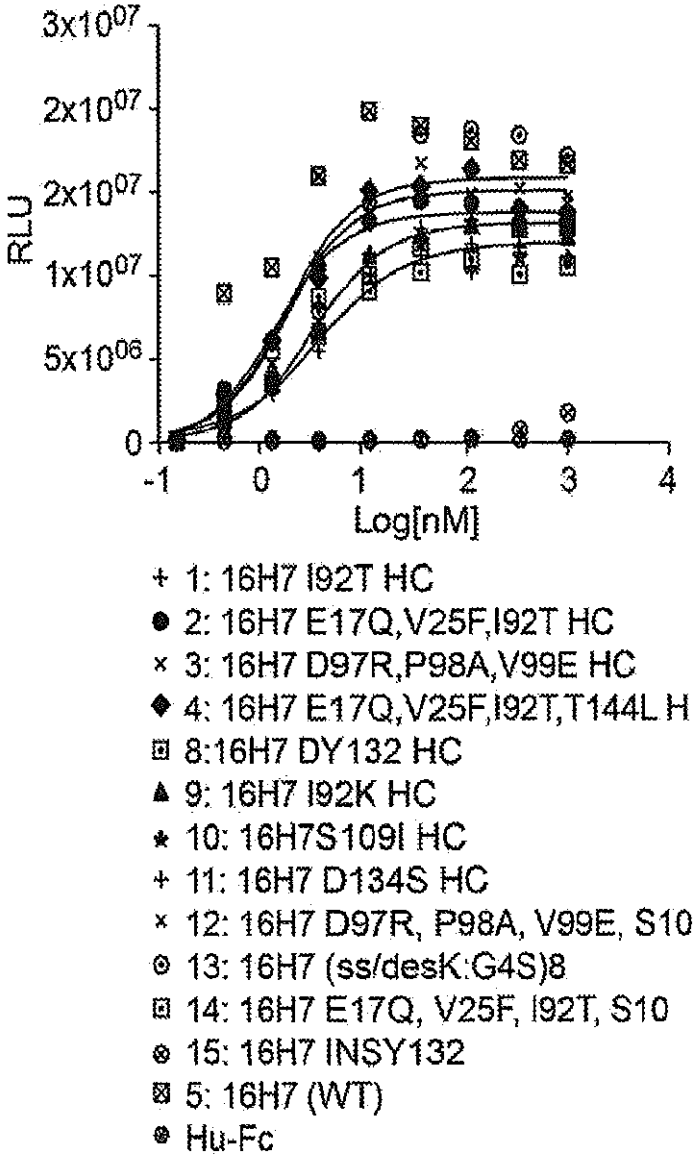

3x10^07
2x10^07
2x10^07
1x10^07
5x10^06
0
RLU
-1
0
1
2
3
4
Log[nM]
+ 1: 16H7 I92T HC
● 2: 16H7 E17Q,V25F,I92T HC
× 3: 16H7 D97R,P98A,V99E HC
◆ 4: 16H7 E17Q,V25F,I92T,T144L H
⊡ 8:16H7 DY132 HC
▲ 9: 16H7 I92K HC
✱ 10: 16H7S109I HC
+ 11: 16H7 D134S HC
× 12: 16H7 D97R, P98A, V99E, S10
⊙ 13: 16H7 (ss/desK:G4S)8
⊡ 14: 16H7 E17Q, V25F, I92T, S10
⊗ 15: 16H7 INSY132
⊠ 5: 16H7 (WT)
⊛ Hu-Fc

FIG. 32B

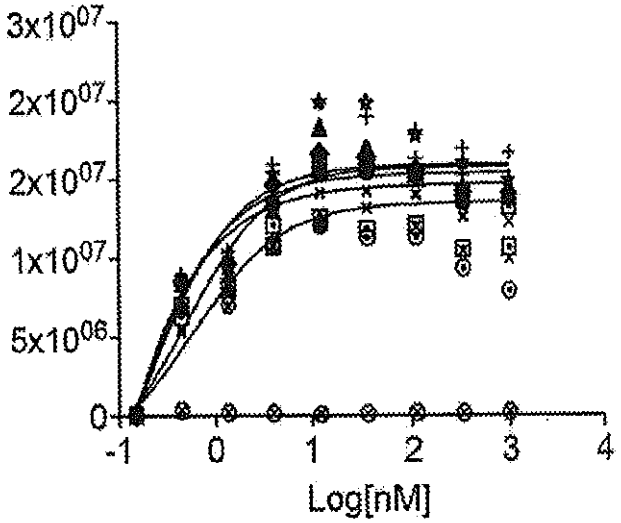

3x10^07
2x10^07
2x10^07
1x10^07
5x10^06
0
-1
0
1
2
3
4
Log[nM]
16: 16H7 V25F HC
17: 16H7 V25F, I92T HC
18: 16H7 D58Y LC
19: 16H7 D58A LC
20: 16H7 D58A, D110A LC
21: 16H7 D110A LC
22: 16H7 D17K LC
5: 16H7 (WT)
6: 22H5 S134A LC
7: 22H5 N111Q HC
23: 22H5 (WT)
Neg Fc

FIG. 32C

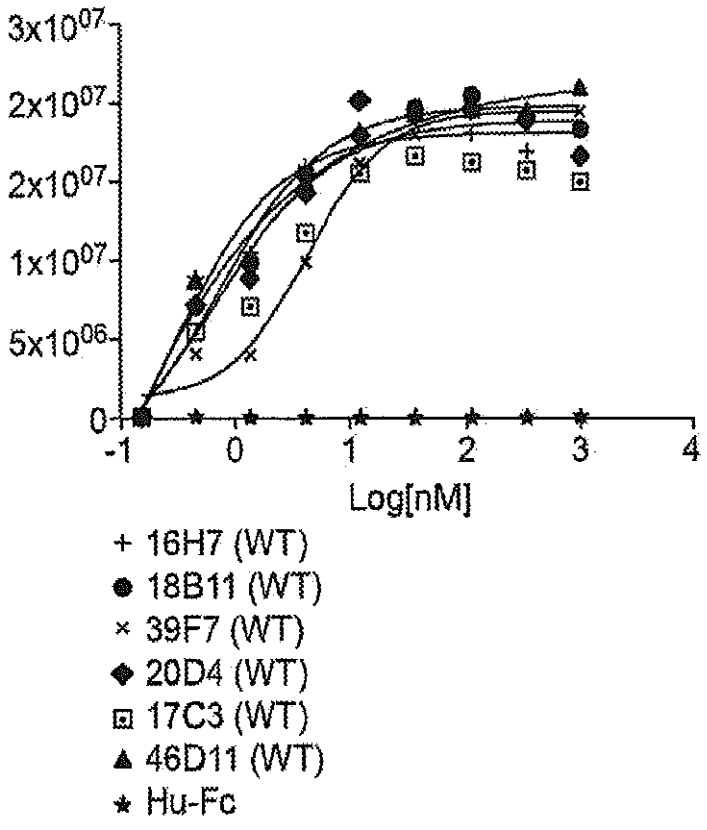

3x10^07
2x10^07
2x10^07
1x10^07
5x10^06
0
-1
0
1
2
3
4
Log[nM]
16H7 (WT)
18B11 (WT)
39F7 (WT)
20D4 (WT)
17C3 (WT)
46D11 (WT)
Hu-Fc

FIG. 33

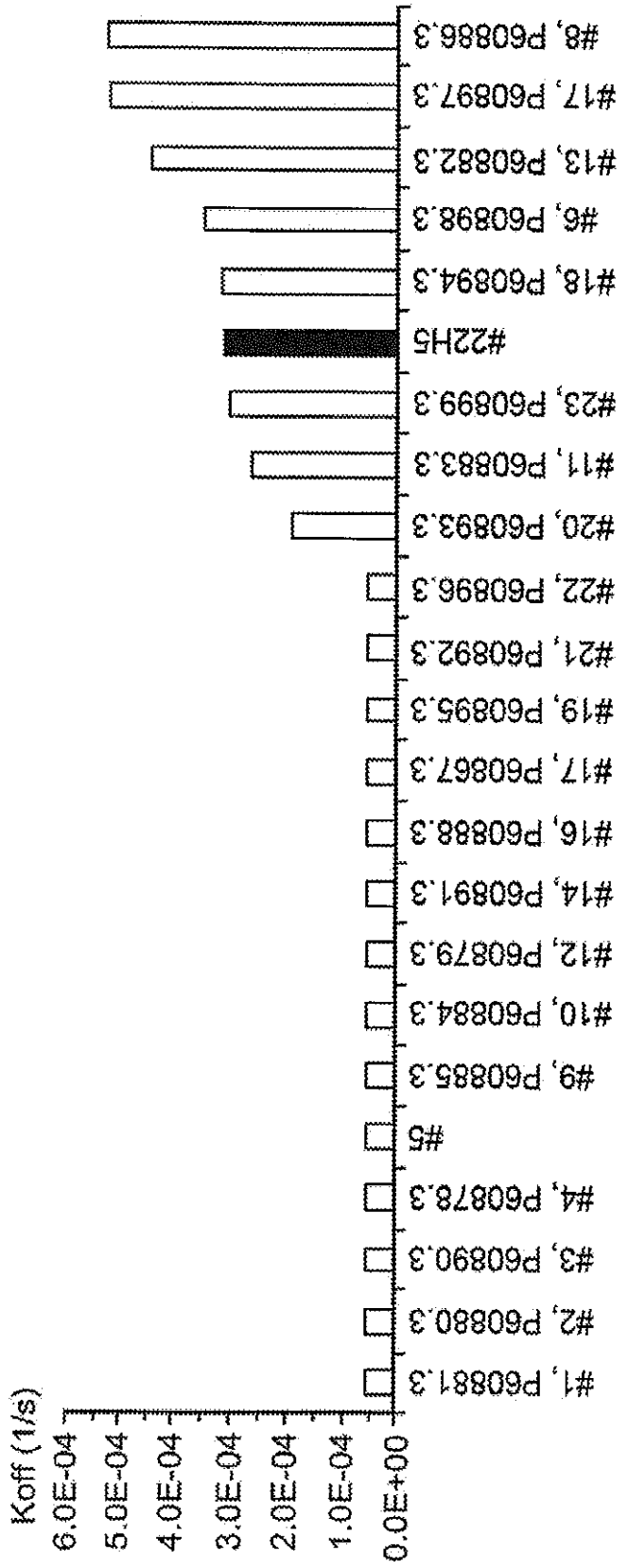

Koff (1/s)
6.0E-04
5.0E-04
4.0E-04
3.0E-04
2.0E-04
1.0E-04
0.0E+00
#1, P60881.3
#2, P60880.3
#3, P60890.3
#4, P60878.3
#5
#9, P60885.3
#10, P60884.3
#12, P60879.3
#14, P60891.3
#16, P60888.3
#17, P60867.3
#19, P60895.3
#21, P60892.3
#22, P60896.3
#20, P60893.3
#11, P60883.3
#23, P60899.3
#22H5
#18, P60894.3
#6, P60898.3
#13, P60882.3
#17, P60897.3
#8, P60886.3

FIG. 34A

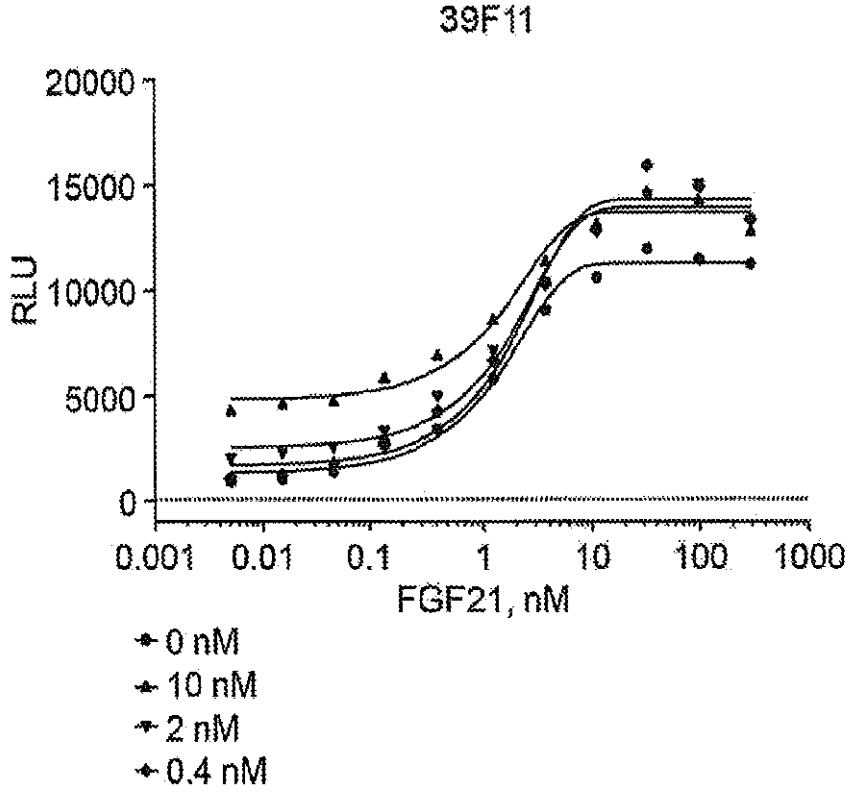


FIG. 34B

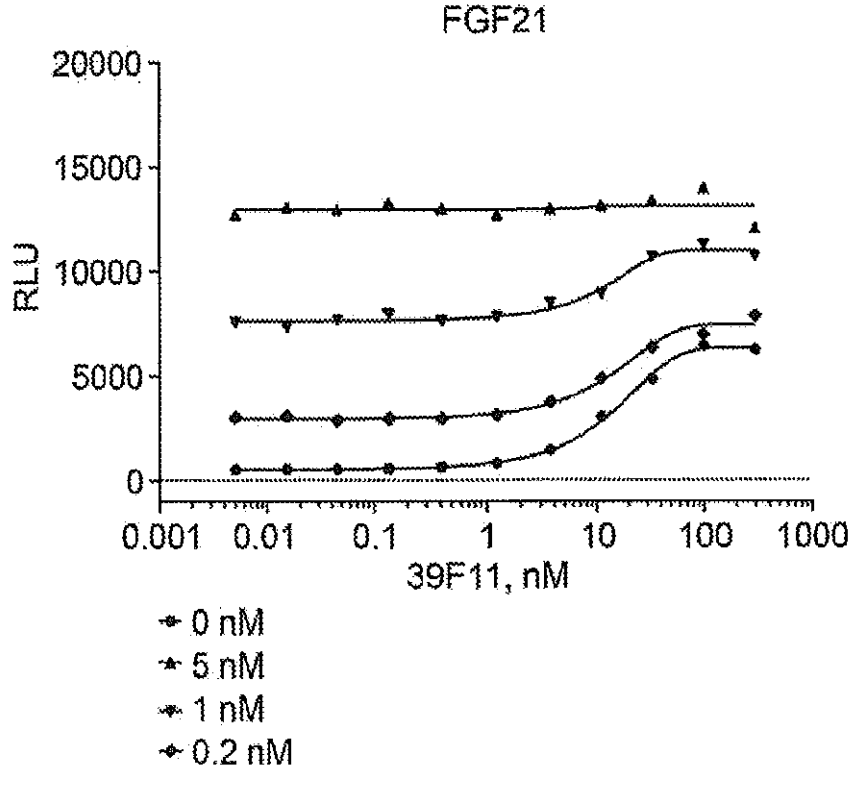


FIG. 35A

16H7

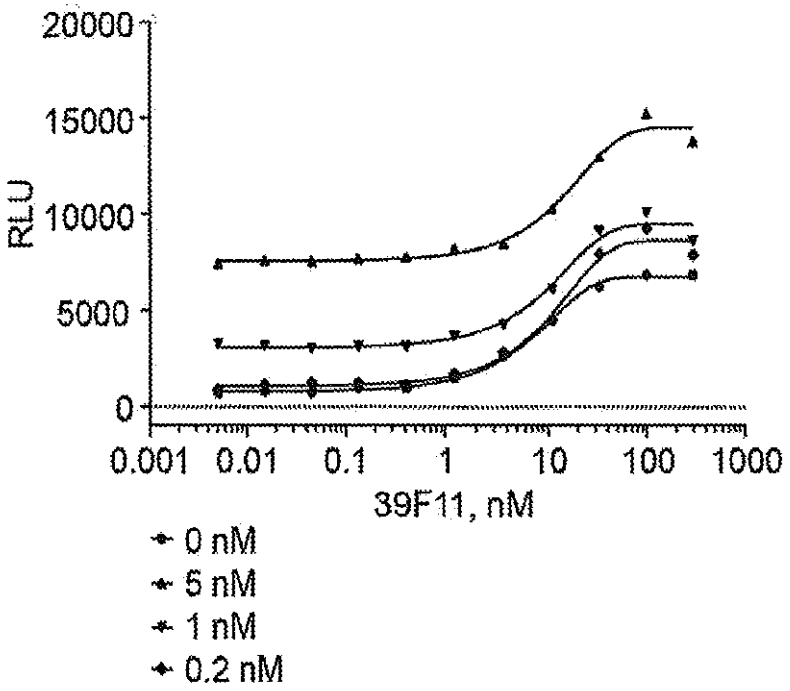


FIG. 35B

39F11

