Figure 1

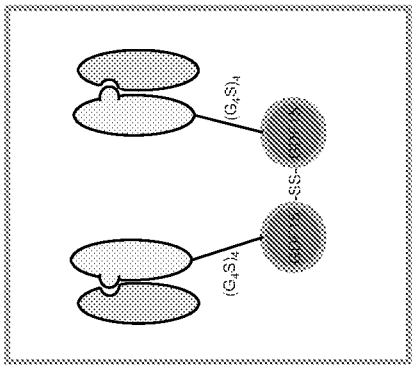


Figure 2

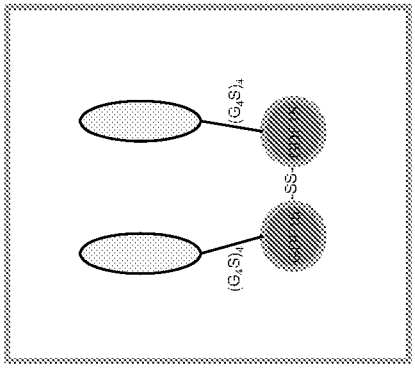


Figure 3

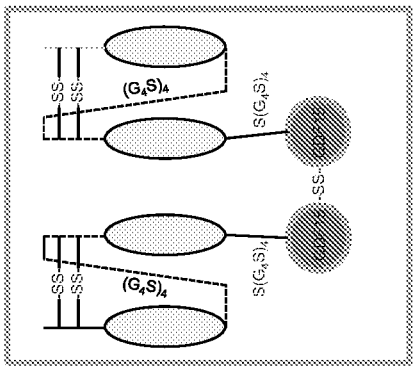


Figure 4

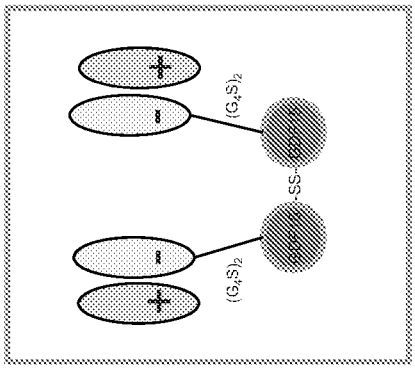


Figure 5

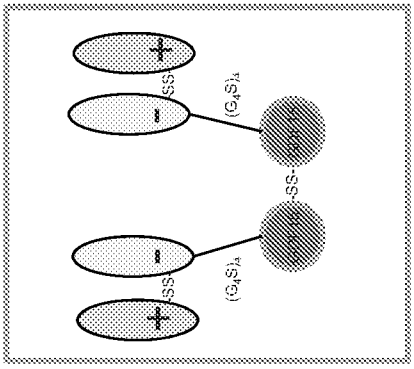


Figure 6

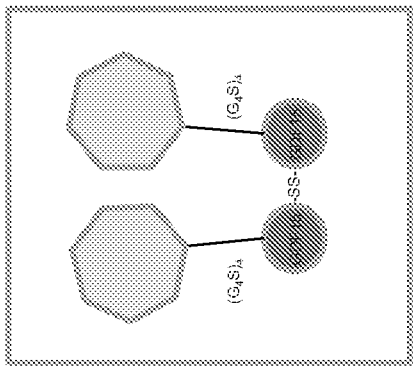


Figure 7

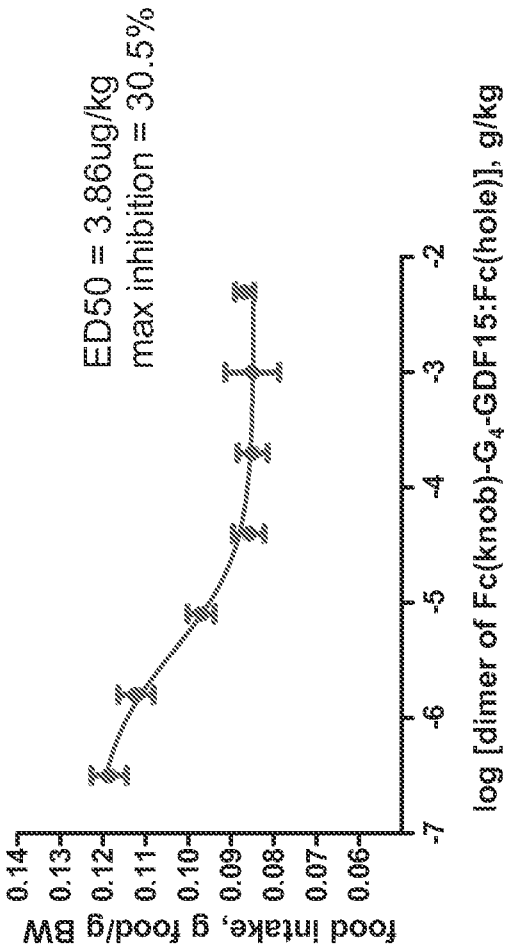

Food intake assay
Dimer of Fc(knob)-G4-GDF15:Fc(hole)
ED50 = 3.86ug/kg
max inhibition = 30.5%
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of Fc(knob)-G4-GDF15:Fc(hole)], g/kg

Figure 8

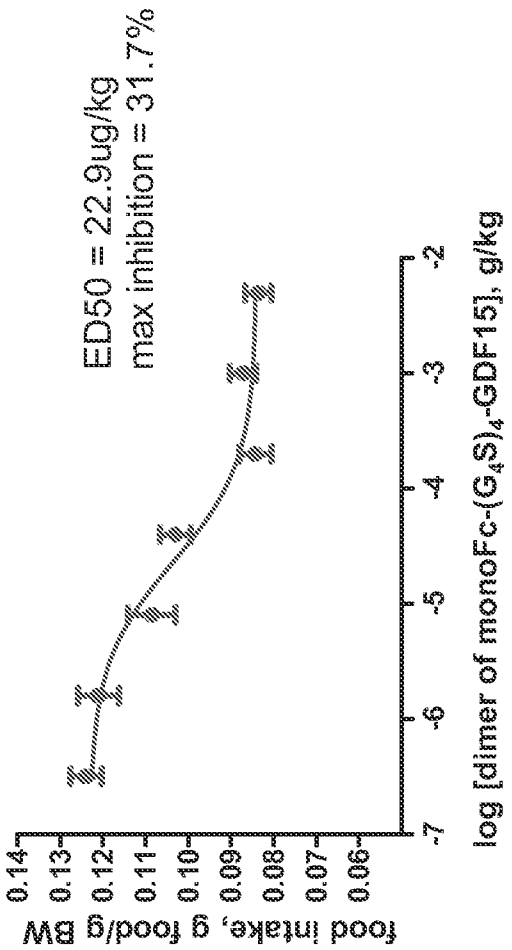

Food intake assay
Dimer of monoFc-(G4S)4-GDF15
ED50 = 22.9ug/kg
max inhibition = 31.7%
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of monoFc-(G4S)4-GDF15], g/kg

Figure 9

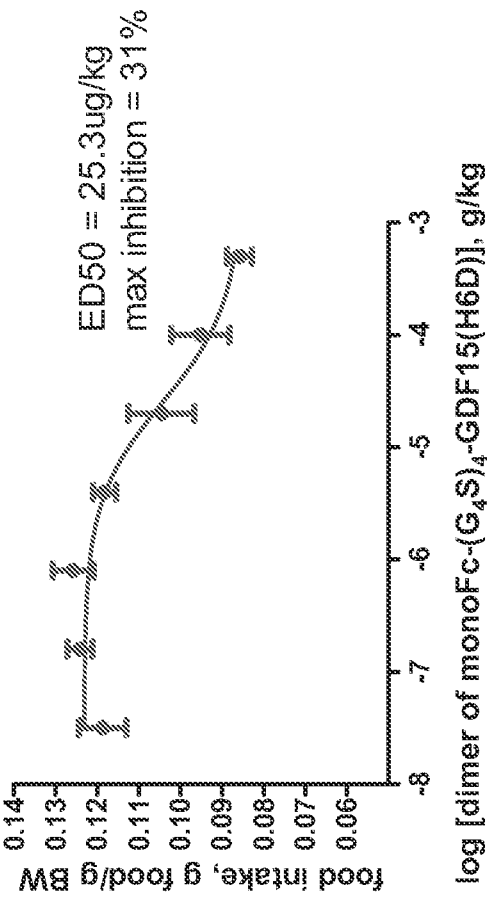

Food intake assay
Dimer of monoFc-(G4S)4-GDF15(H6D)
ED50 = 25.3ug/kg
max inhibition = 31%
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-8
-7
-6
-5
-4
-3
log [dimer of monoFc-(G4S)4-GDF15(H6D)], g/kg

Figure 10

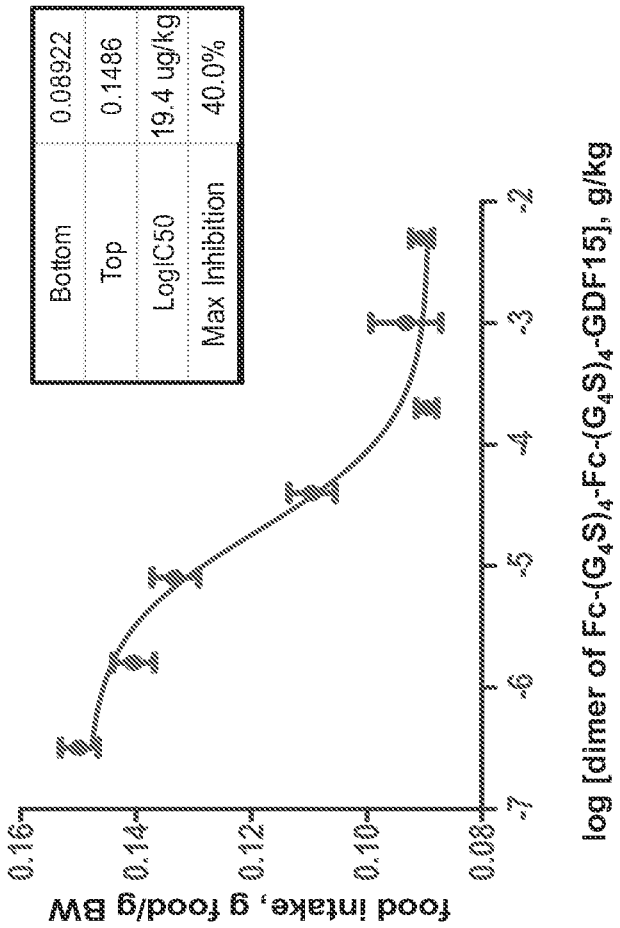

Food intake assay
Dimer of Fc-(G4S)4-Fc-(G4S)4-GDF15
Bottom 0.08922
Top 0.1486
LogIC50 19.4 ug/kg
Max Inhibition 40.0%
food intake, g food/g BW
0.16
0.14
0.12
0.10
0.08
-7
-6
-5
-4
-3
-2
log [dimer of Fc-(G4S)4-Fc-(G4S)4-GDF15], g/kg

Figure 11

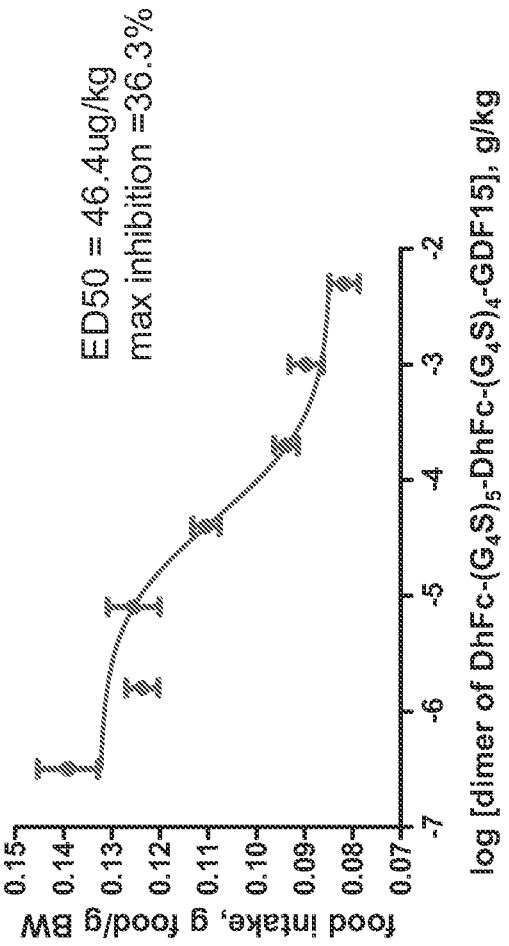

Food intake assay
Dimer of DhFc-(G4S)5-DhFc-(G4S)4-GDF15
ED50 = 46.4ug/kg
max inhibition =36.3%
food intake, g food/g BW
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
-7
-6
-5
-4
-3
-2
log [dimer of DhFc-(G4S)5-DhFc-(G4S)4-GDF15], g/kg

Figure 12

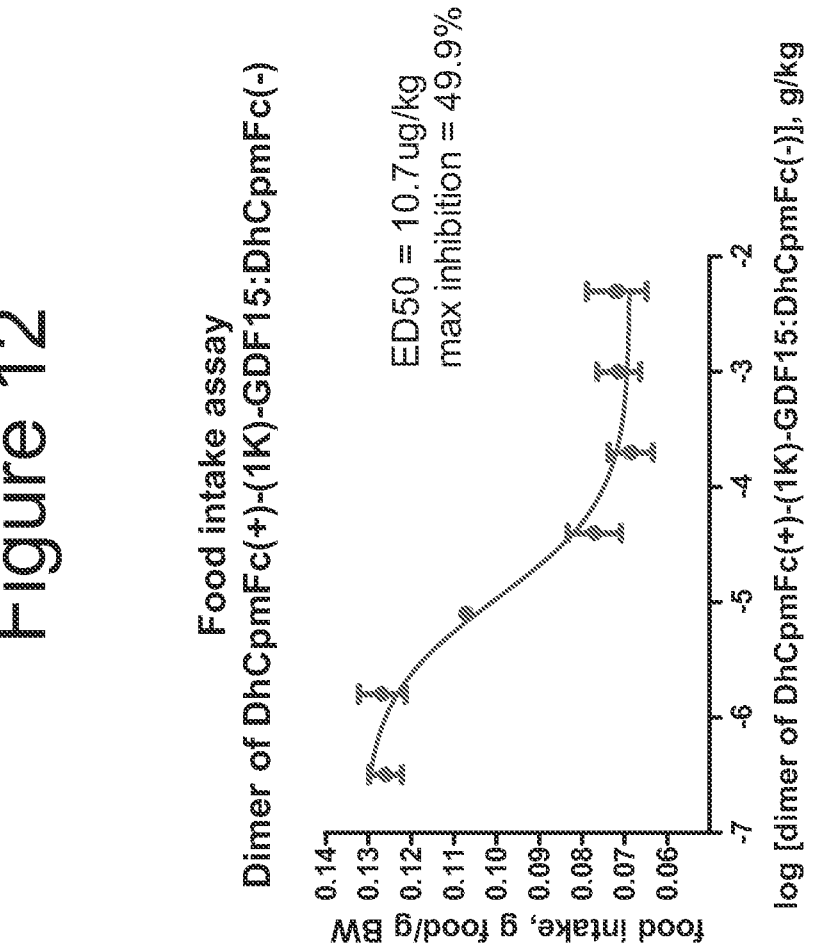

Food intake assay
Dimer of DhCpmFc(+)-(1K)-GDF15:DhCpmFc(-)
ED50 = 10.7ug/kg
max inhibition = 49.9%
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(+)-(1K)-GDF15:DhCpmFc(-)], g/kg

Figure 13

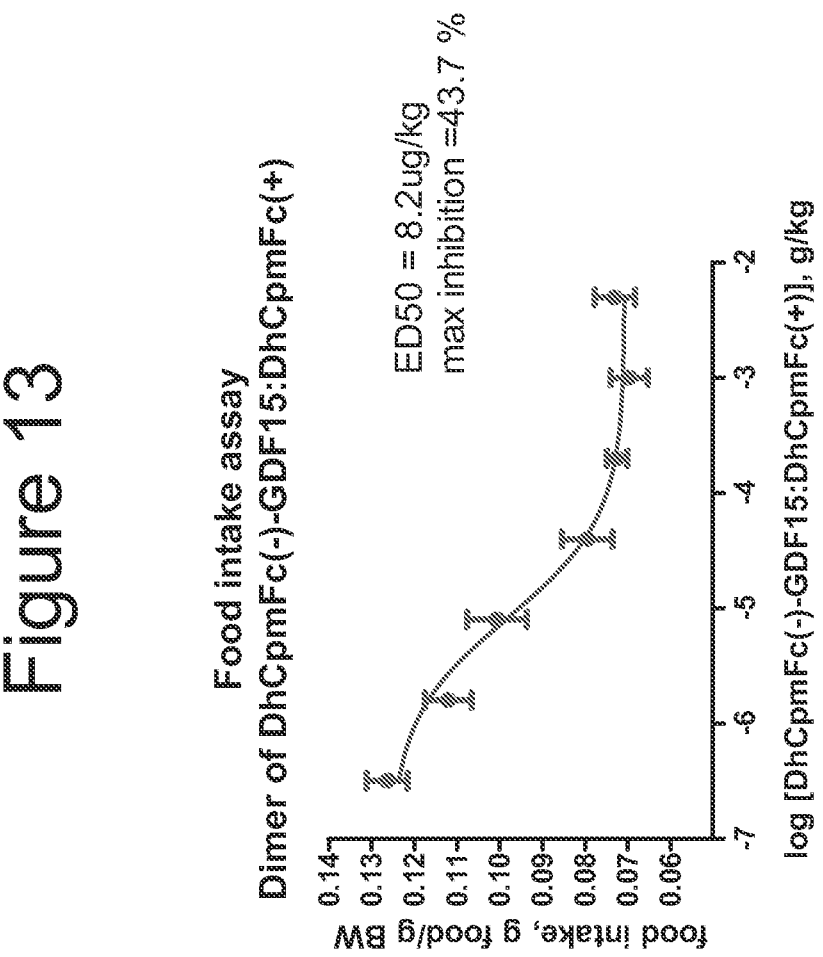

Food intake assay
Dimer of DhCpmFc(-)-GDF15:DhCpmFc(+)
ED50 = 8.2ug/kg
max inhibition =43.7 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [DhCpmFc(-)-GDF15:DhCpmFc(+)], g/kg

Figure 14

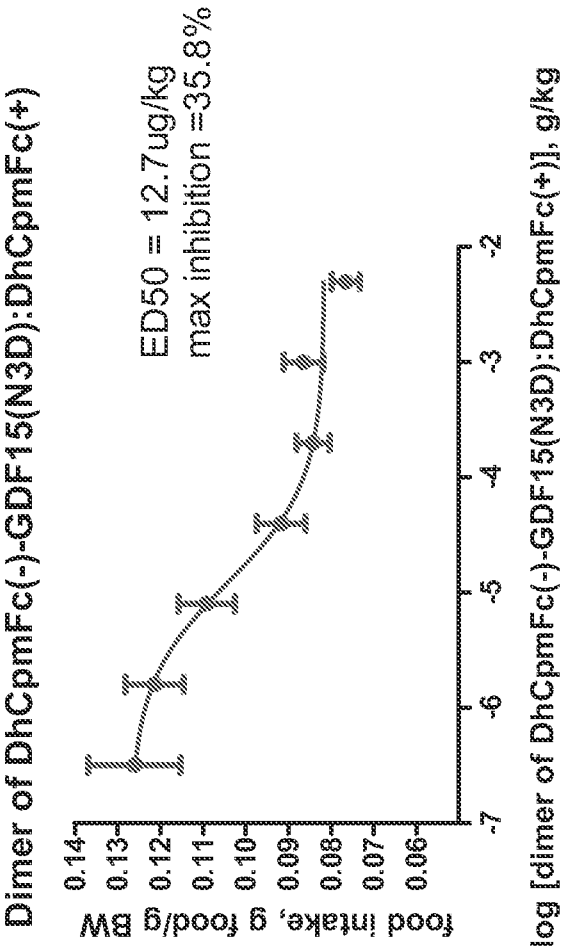

Food intake assay
Dimer of DhCpmFc(-)-GDF15(N3D):DhCpmFc(+)
ED50 = 12.7ug/kg
max inhibition =35.8%
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-GDF15(N3D):DhCpmFc(+)], g/kg

Figure 15

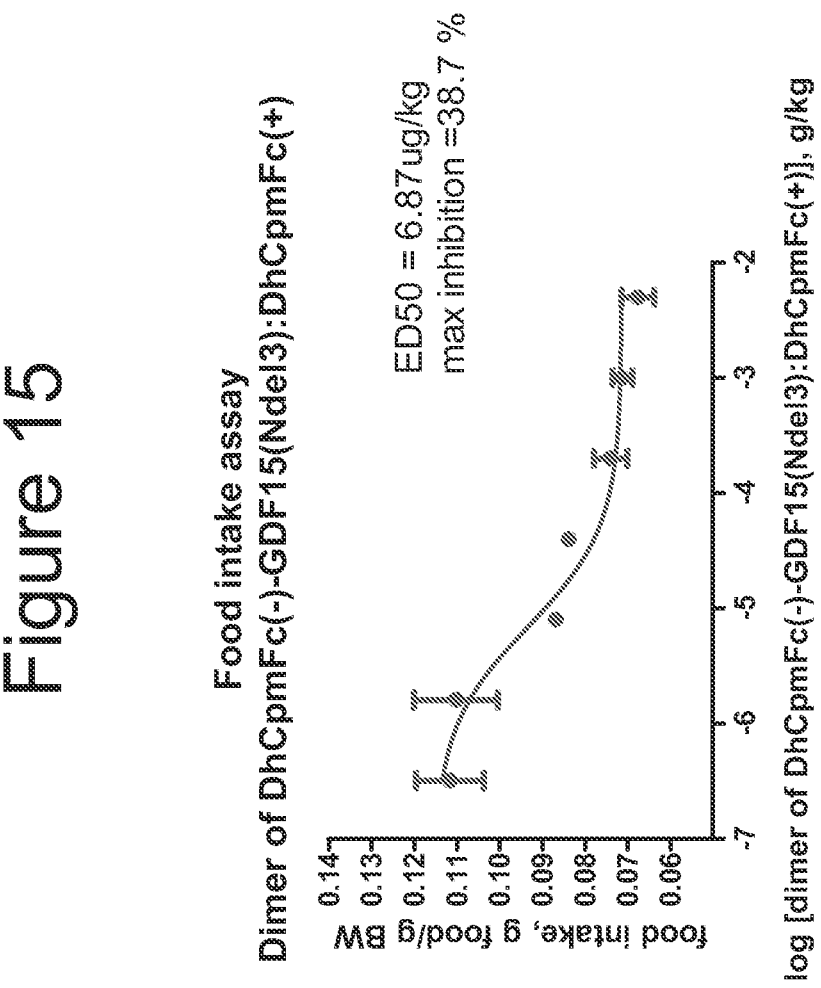

Food intake assay
Dimer of DhCpmFc(-)-GDF15(Ndel3):DhCpmFc(+)
ED50 = 6.87ug/kg
max inhibition =38.7 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-GDF15(Ndel3):DhCpmFc(+)], g/kg

Figure 16

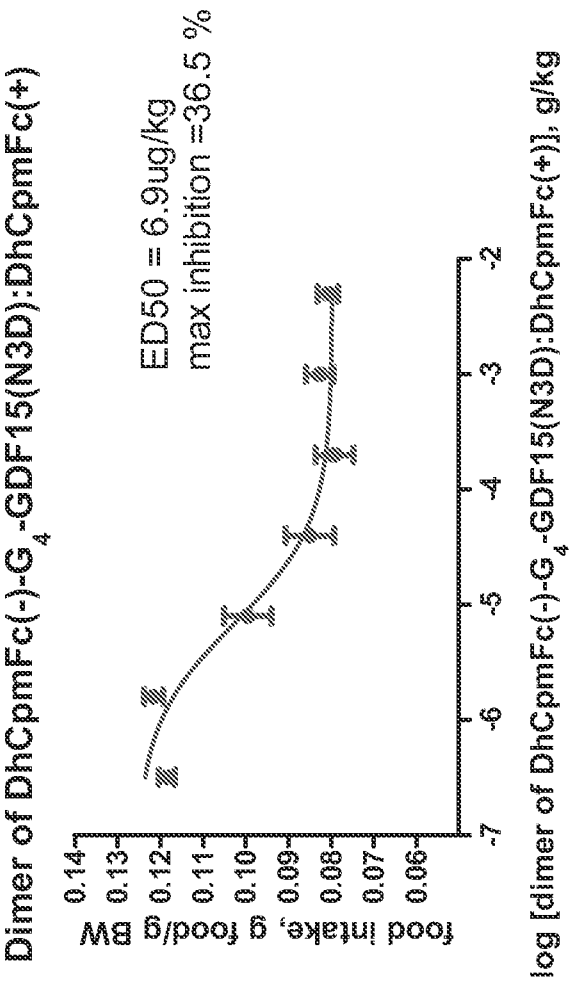

Food intake assay
Dimer of DhCpmFc(-)-G4-GDF15(N3D):DhCpmFc(+)
ED50 = 6.9ug/kg
max inhibition =36.5 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-G4-GDF15(N3D):DhCpmFc(+)], g/kg

Figure 17

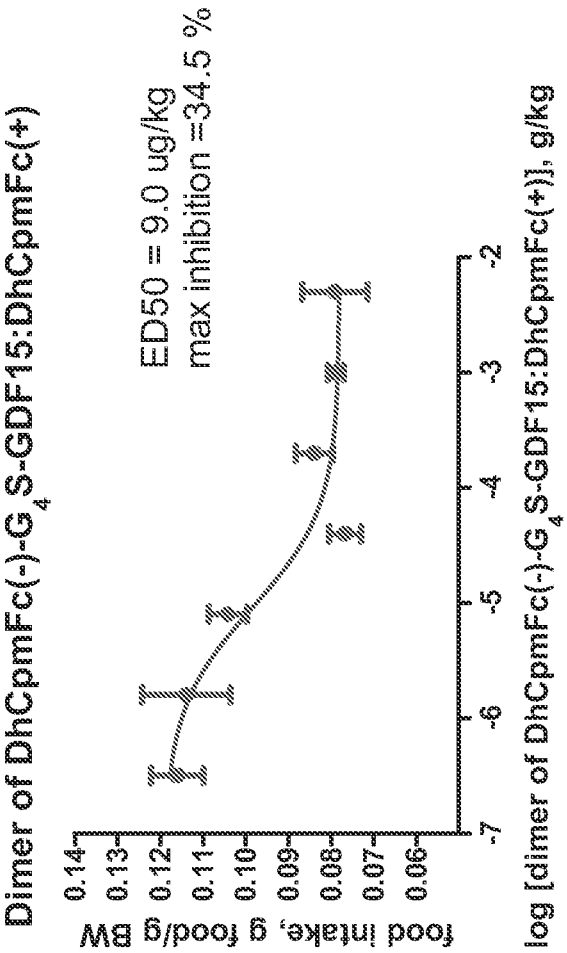

Food intake assay
Dimer of DhCpmFc(-)-G4S-GDF15:DhCpmFc(+)
ED50 = 9.0 ug/kg
max inhibition =34.5 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-G4S-GDF15:DhCpmFc(+)], g/kg

Figure 18

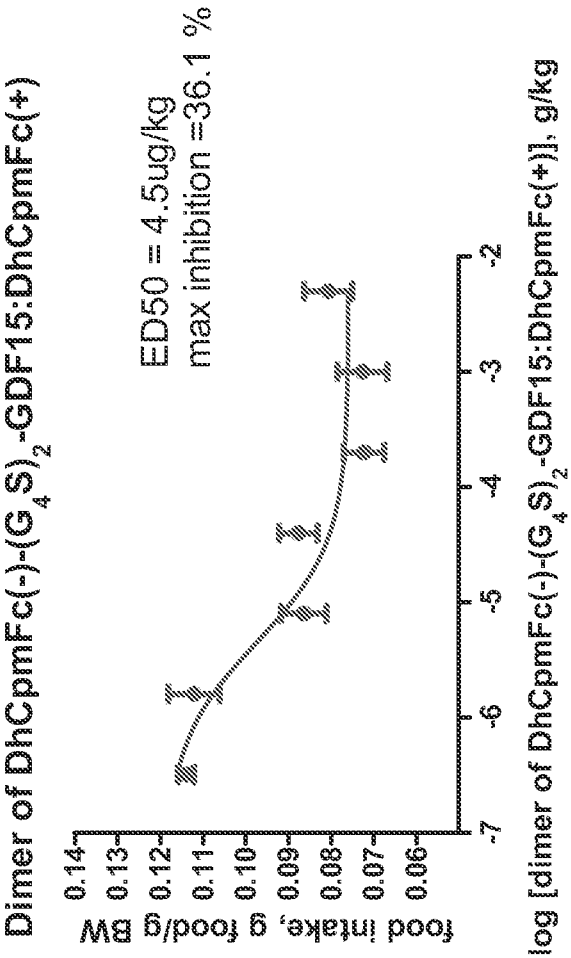

Food intake assay
Dimer of DhCpmFc(-)-(G4S)2-GDF15:DhCpmFc(+)
ED50 = 4.5ug/kg
max inhibition =36.1 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-(G4S)2-GDF15:DhCpmFc(+)], g/kg

Figure 19

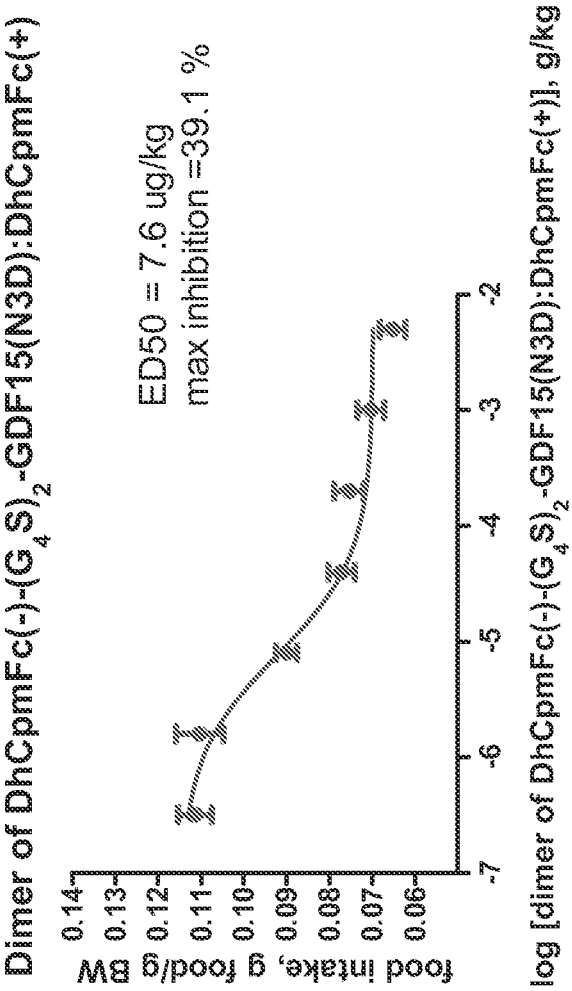

Food intake assay
Dimer of DhCpmFc(-)-(G4S)2-GDF15(N3D):DhCpmFc(+)
ED50 = 7.6 ug/kg
max inhibition =39.1 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-(G4S)2-GDF15(N3D):DhCpmFc(+)], g/kg

Figure 20

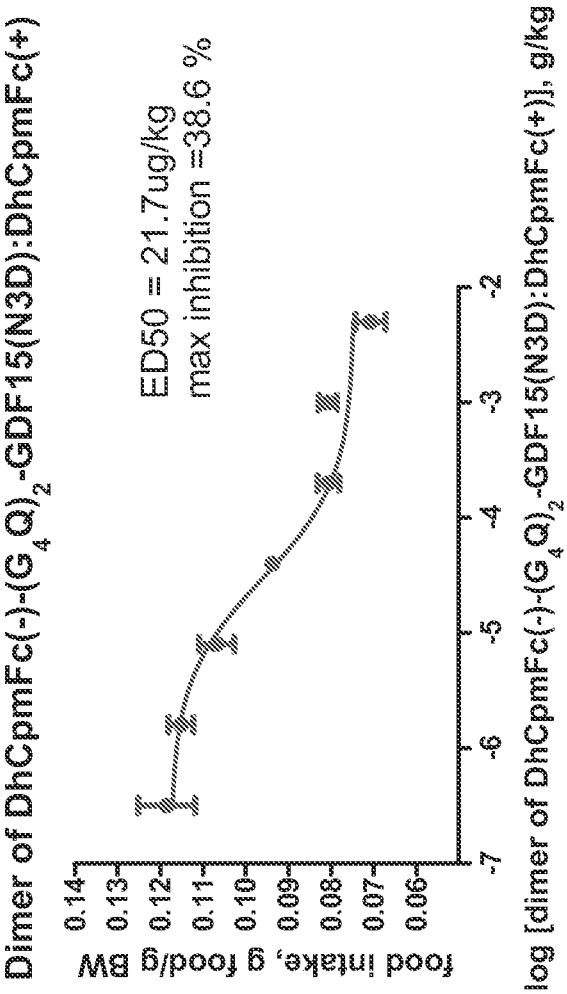

Food intake assay
Dimer of DhCpmFc(-)-(G4Q)2-GDF15(N3D):DhCpmFc(+)
ED50 = 21.7ug/kg
max inhibition =38.6 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-(G4Q)2-GDF15(N3D):DhCpmFc(+)], g/kg

Figure 21

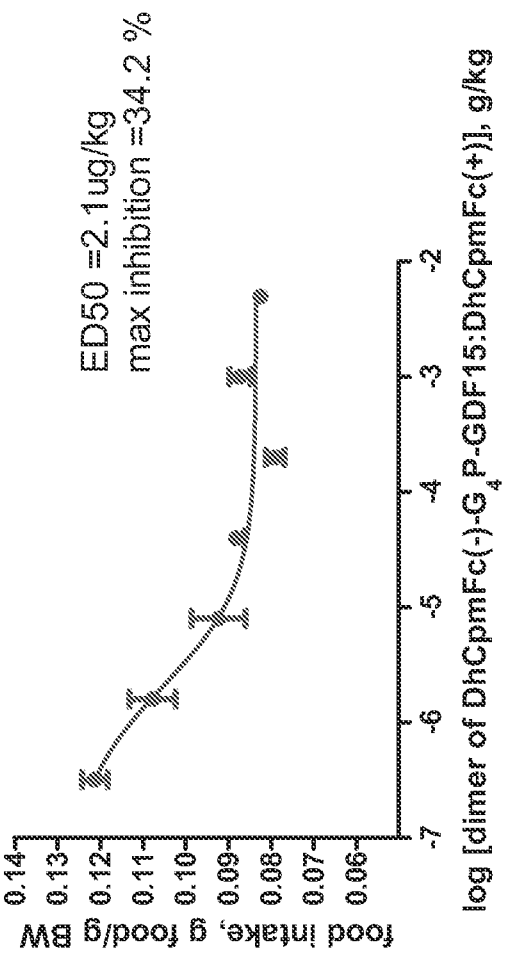

Food intake assay
Dimer of DhCpmFc(-)-G4P-GDF15:DhCpmFc(+)
ED50 =2.1ug/kg
max inhibition =34.2 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-G4P-GDF15:DhCpmFc(+)], g/kg

Figure 22

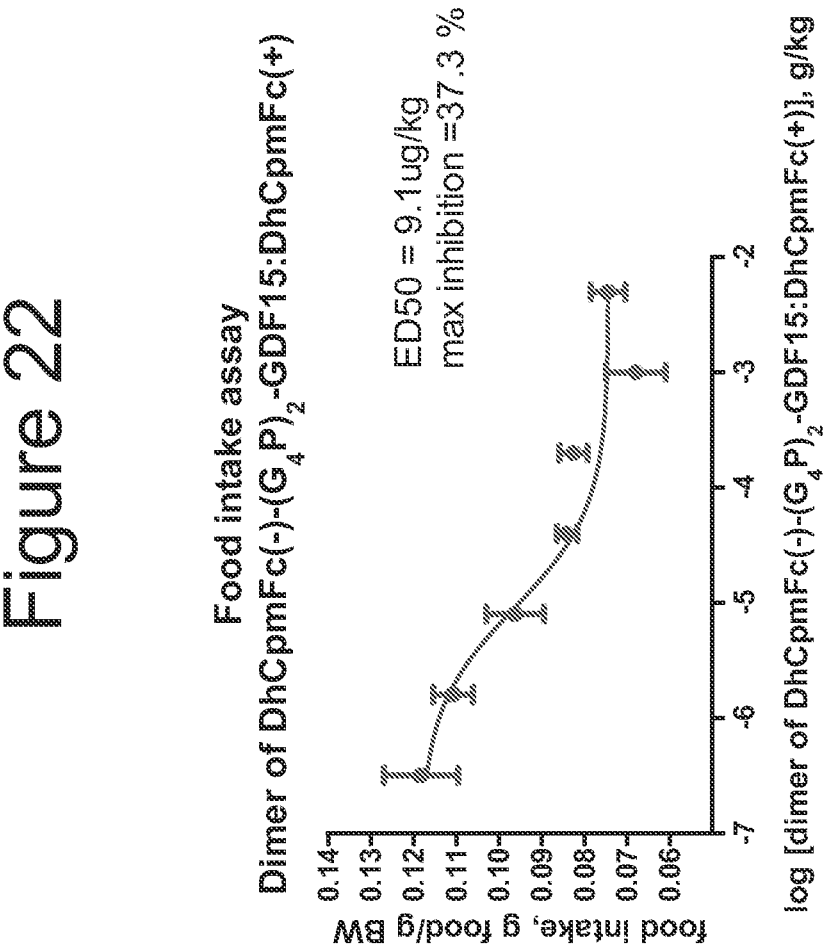

Food intake assay
Dimer of DhCpmFc(-)-(G4P)2-GDF15:DhCpmFc(+)
ED50 = 9.1ug/kg
max inhibition =37.3 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-(G4P)2-GDF15:DhCpmFc(+)], g/kg

Figure 23

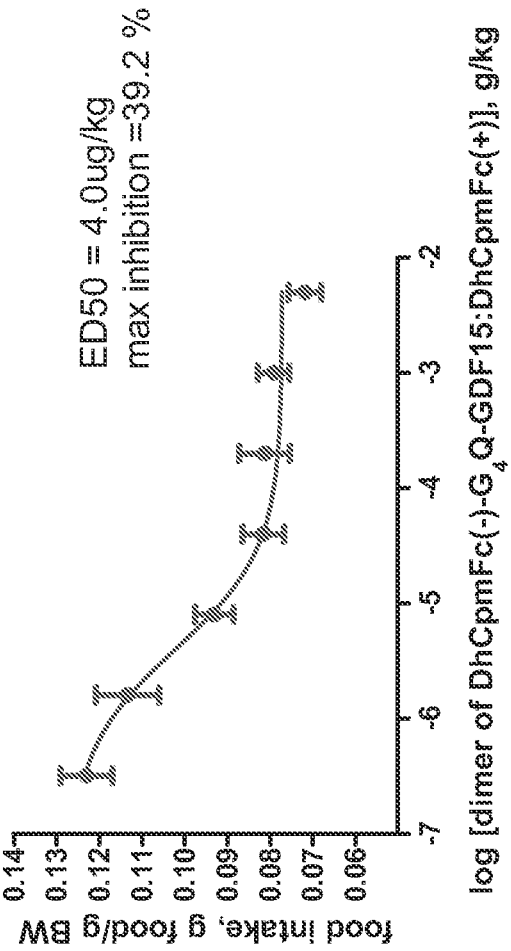

Food intake assay
Dimer of DhCpmFc(-)-G4Q-GDF15:DhCpmFc(+)
ED50 = 4.0ug/kg
max inhibition =39.2 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-G4Q-GDF15:DhCpmFc(+)], g/kg

Figure 24

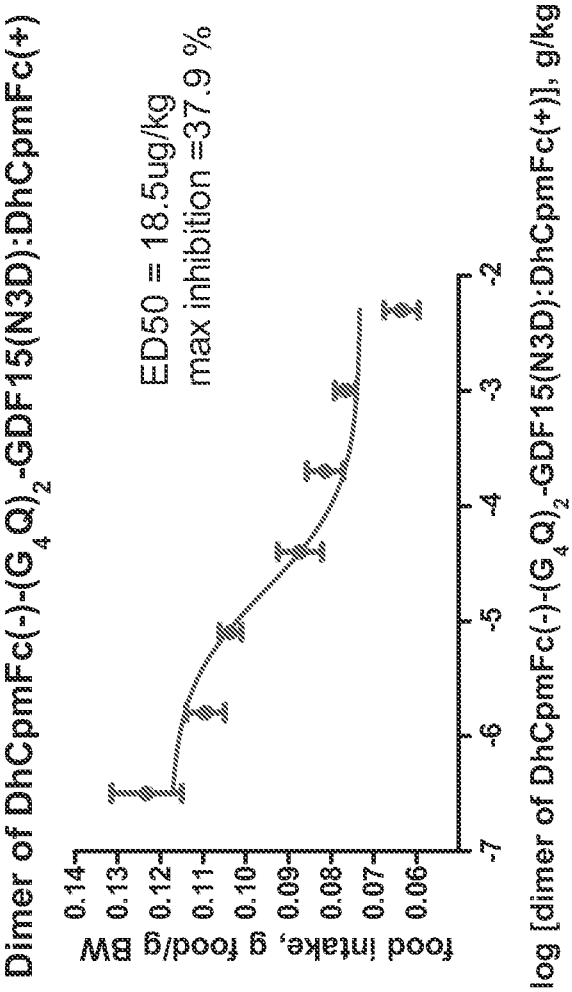

Food intake assay
Dimer of DhCpmFc(-)-(G4Q)2-GDF15(N3D):DhCpmFc(+)
ED50 = 18.5ug/kg
max inhibition =37.9 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-(G4Q)2-GDF15(N3D):DhCpmFc(+)], g/kg

Figure 25

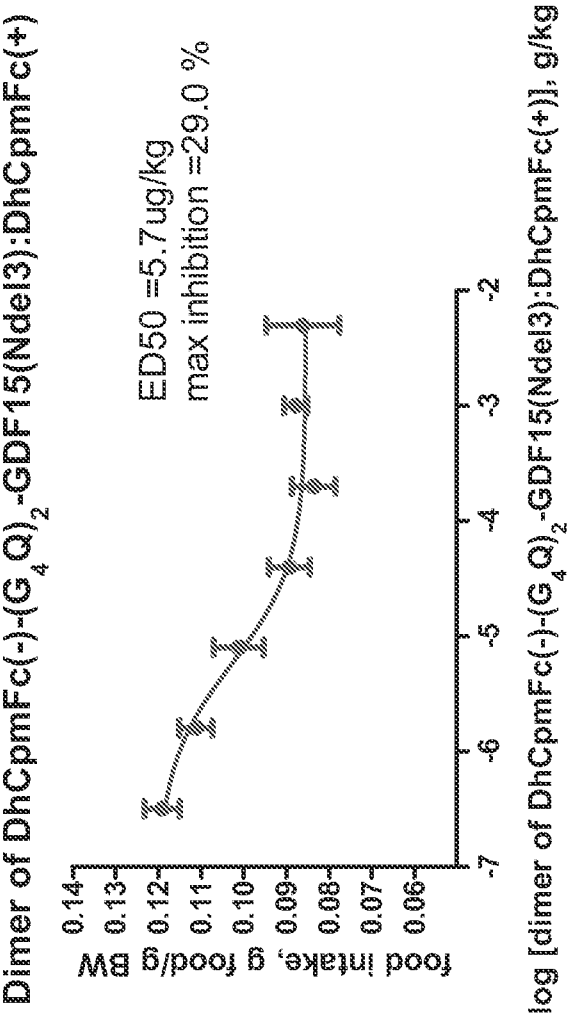

Food intake assay
Dimer of DhCpmFc(-)-(G4Q)2-GDF15(Ndel3):DhCpmFc(+)
ED50 =5.7ug/kg
max inhibition =29.0 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)-(G4Q)2-GDF15(Ndel3):DhCpmFc(+)], g/kg

Figure 26

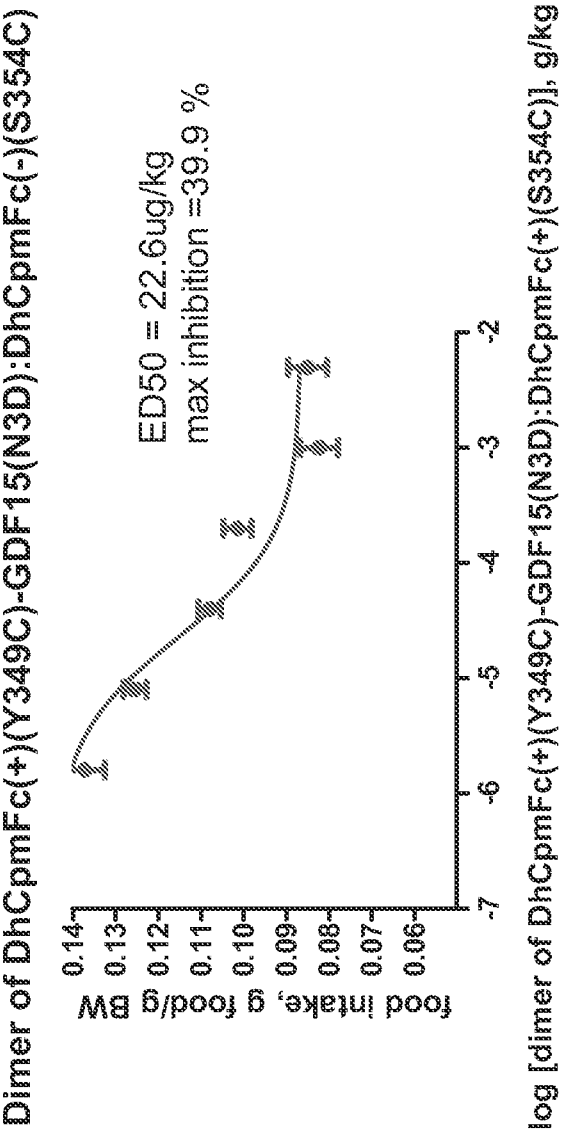

Food intake assay
Dimer of DhCpmFc(+)(Y349C)-GDF15(N3D):DhCpmFc(-)(S354C)
ED50 = 22.6ug/kg
max inhibition =39.9 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(+)(Y349C)-GDF15(N3D):DhCpmFc(+)(S354C)], g/kg

Figure 27

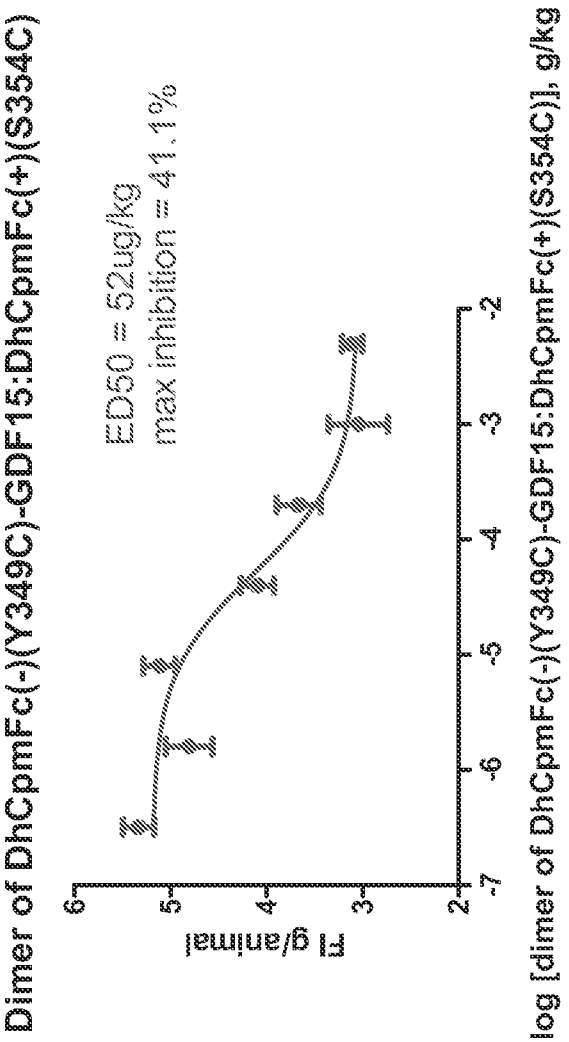

Food intake assay
Dimer of DhCpmFc(-)(Y349C)-GDF15:DhCpmFc(+)(S354C)
ED50 = 52ug/kg
max inhibition = 41.1%
FI g/animal
6
5
4
3
2
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(Y349C)-GDF15:DhCpmFc(+)(S354C)], g/kg

Figure 28

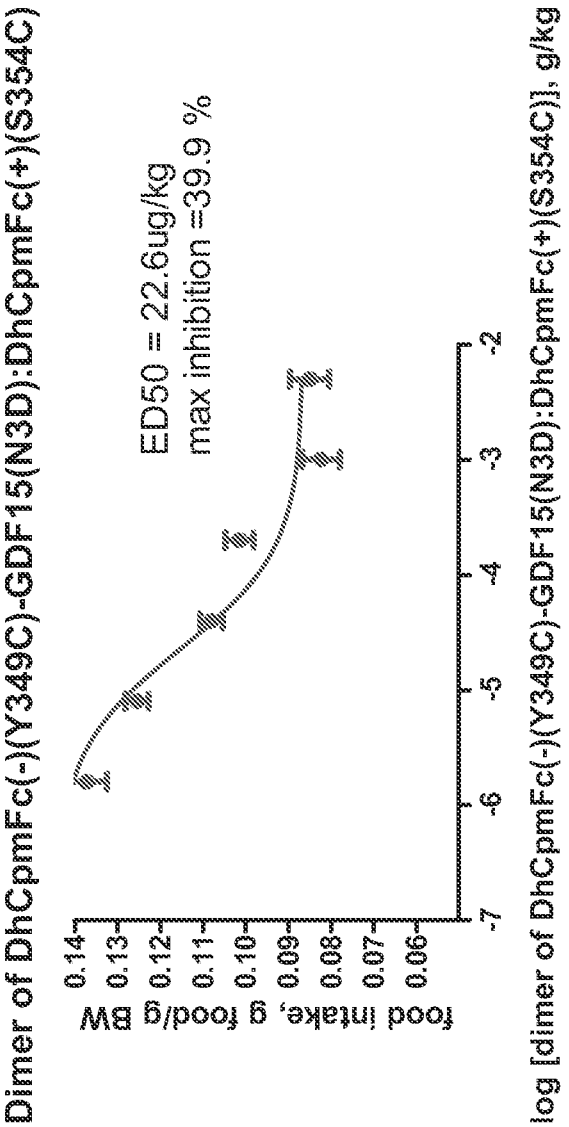

Food intake assay
Dimer of DhCpmFc(-)(Y349C)-GDF15(N3D):DhCpmFc(+)(S354C)
ED50 = 22.6ug/kg
max inhibition =39.9 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(Y349C)-GDF15(N3D):DhCpmFc(+)(S354C)], g/kg

Figure 29

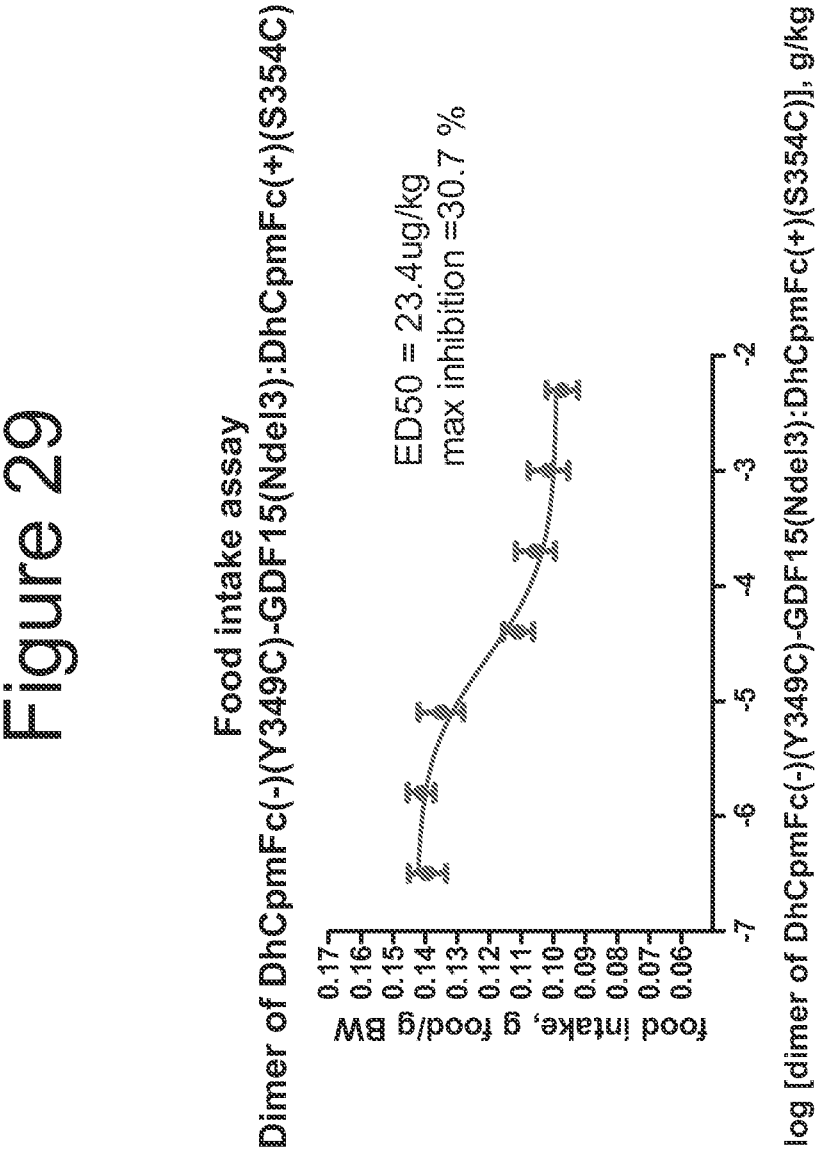

Food intake assay
Dimer of DhCpmFc(-)(Y349C)-GDF15(Ndel3):DhCpmFc(+)(S354C)
ED50 = 23.4ug/kg
max inhibition =30.7 %
food intake, g food/g BW
0.17
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(Y349C)-GDF15(Ndel3):DhCpmFc(+)(S354C)], g/kg

Figure 30

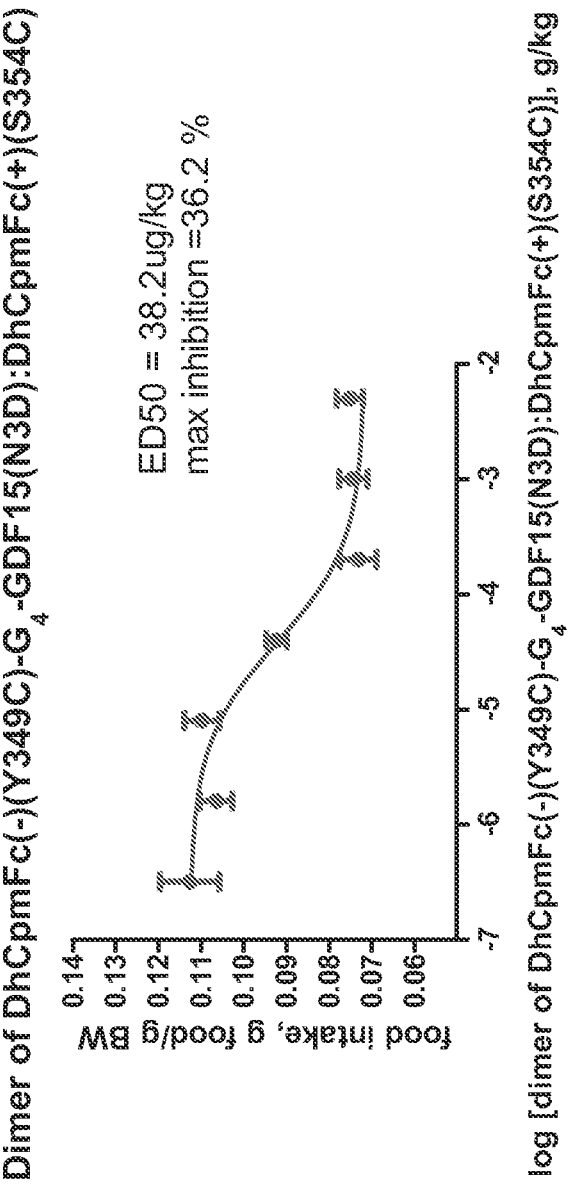

Food intake assay
Dimer of DhCpmFc(-)(Y349C)-G4-GDF15(N3D):DhCpmFc(+)(S354C)
ED50 = 38.2ug/kg
max inhibition =36.2 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(Y349C)-G4-GDF15(N3D):DhCpmFc(+)(S354C)], g/kg

Figure 31

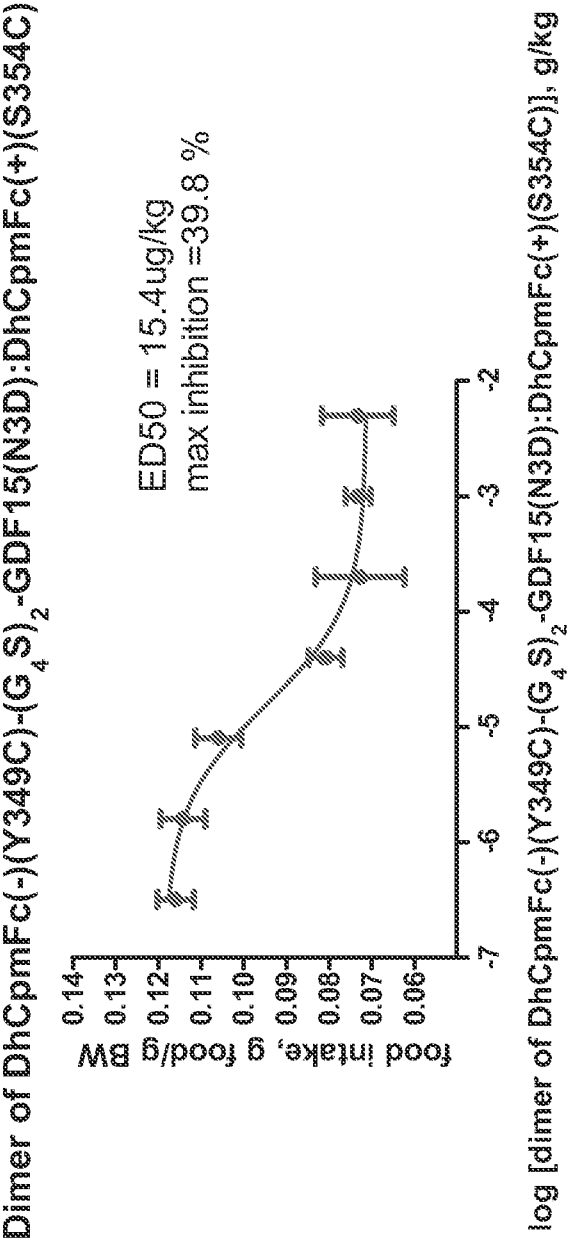

Food intake assay
Dimer of DhCpmFc(-)(Y349C)-(G4S)2-GDF15(N3D):DhCpmFc(+)(S354C)
ED50 = 15.4ug/kg
max inhibition =39.8 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(Y349C)-(G4S)2-GDF15(N3D):DhCpmFc(+)(S354C)], g/kg

Figure 32

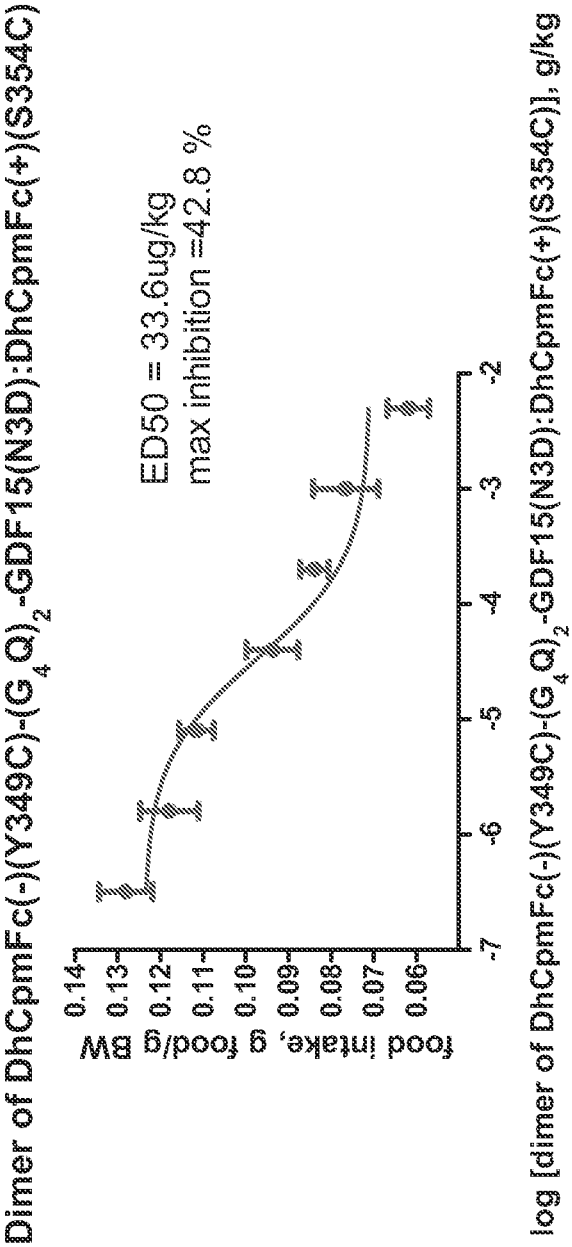

Food intake assay
Dimer of DhCpmFc(-)(Y349C)-(G4Q)2-GDF15(N3D):DhCpmFc(+)(S354C)
ED50 = 33.6ug/kg
max inhibition =42.8 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(Y349C)-(G4Q)2-GDF15(N3D):DhCpmFc(+)(S354C)], g/kg

Figure 33

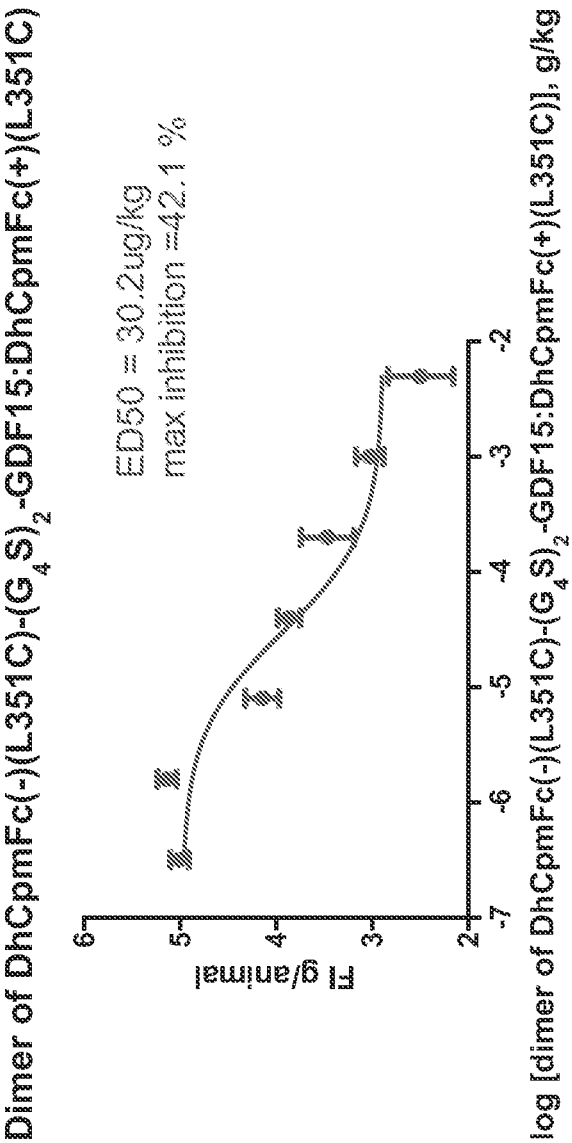

Food intake assay
Dimer of DhCpmFc(-)(L351C)-(G4S)2-GDF15:DhCpmFc(+)(L351C)
ED50 = 30.2ug/kg
max inhibition =42.1 %
Tm g/animal
6
5
4
3
2
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(L351C)-(G4S)2-GDF15:DhCpmFc(+)(L351C)], g/kg

Figure 34

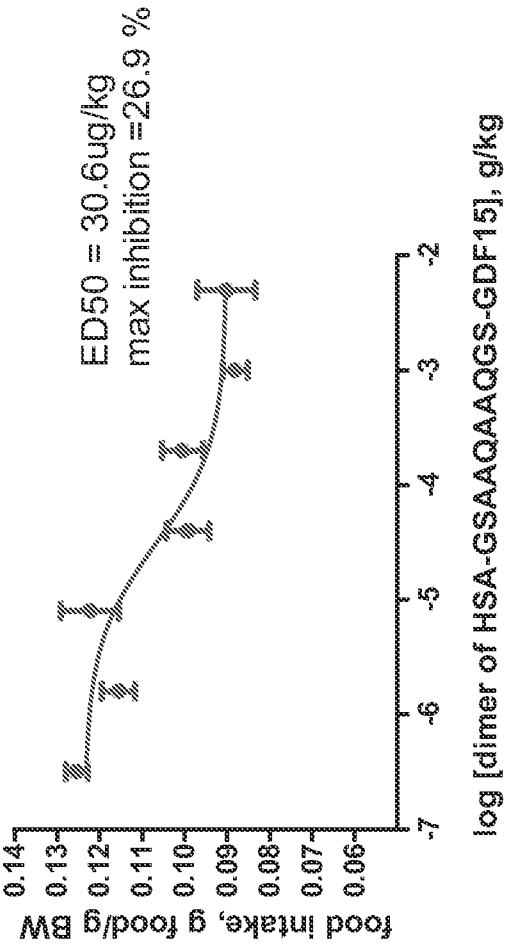

Food intake assay
Dimer of HSA-GSAAQAAQGS-GDF15
ED50 = 30.6ug/kg
max inhibition =26.9 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of HSA-GSAAQAAQGS-GDF15], g/kg

Figure 35

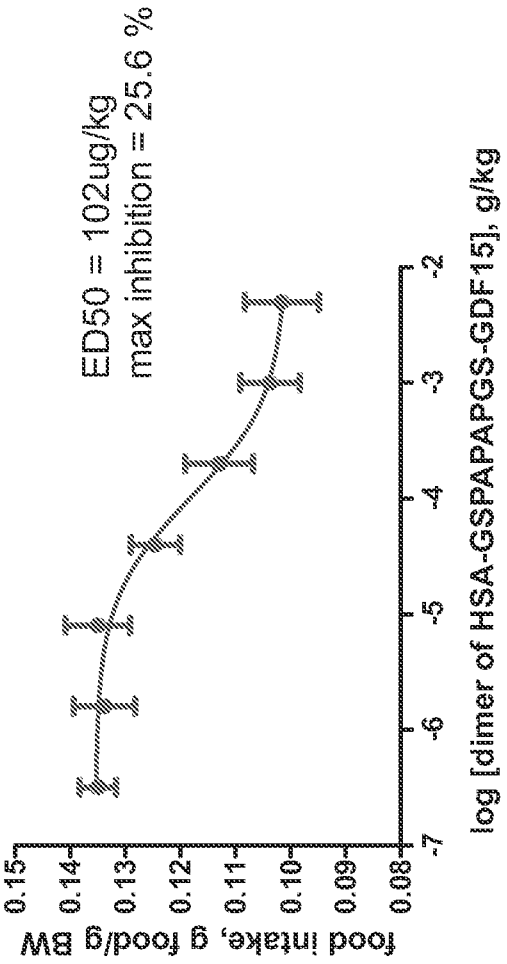

Food intake assay
Dimer of HSA-GSPAPAPGS-GDF15
ED50 = 102ug/kg
max inhibition = 25.6 %
food intake, g food/g BW
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
-7
-6
-5
-4
-3
-2
log [dimer of HSA-GSPAPAPGS-GDF15], g/kg

Figure 36

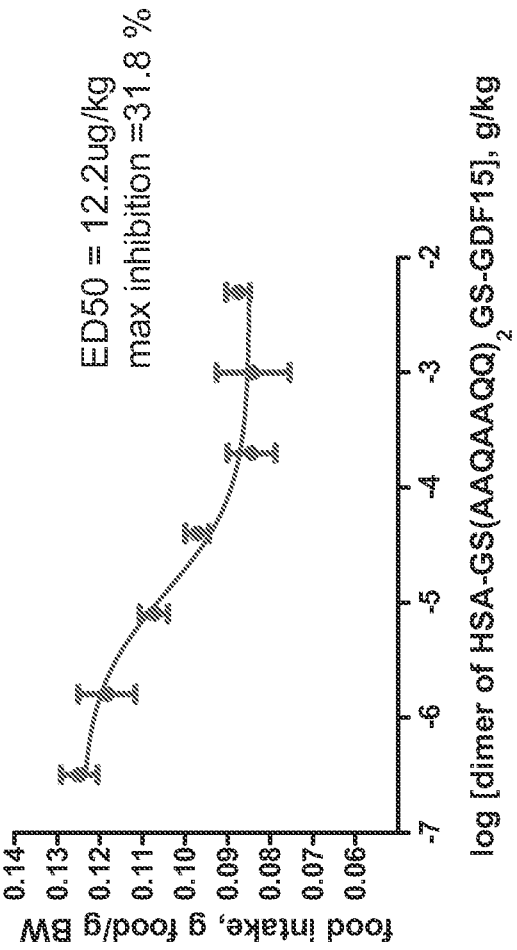

Food intake assay
Dimer of HSA-GS(AAQAAQQ)2 GS-GDF15
ED50 = 12.2ug/kg
max inhibition =31.8 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of HSA-GS(AAQAAQQ)2 GS-GDF15], g/kg

Figure 37

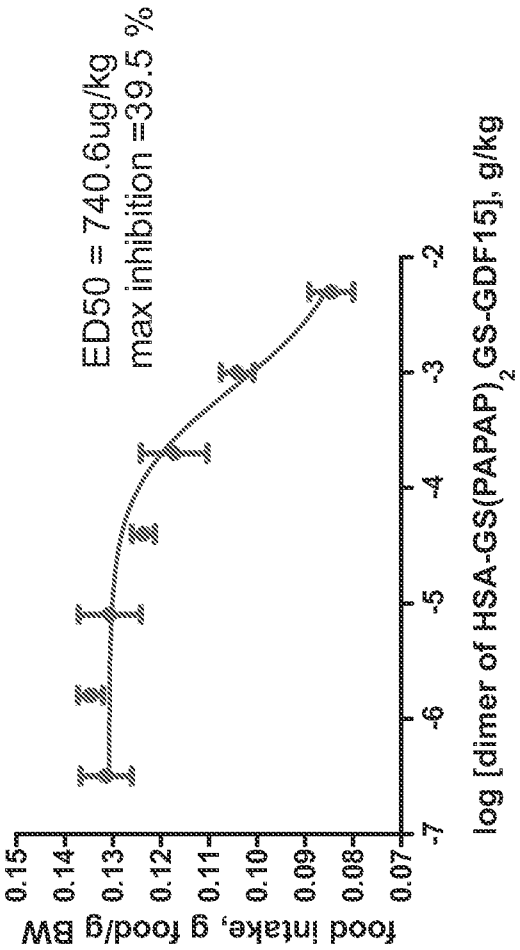

Food intake assay
Dimer of HSA-GS(PAPAP)2GS-GDF15
ED50 = 740.6ug/kg
max inhibition =39.5 %
food intake, g food/g BW
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
-7
-6
-5
-4
-3
-2
log [dimer of HSA-GS(PAPAP)2GS-GDF15], g/kg

Figure 38

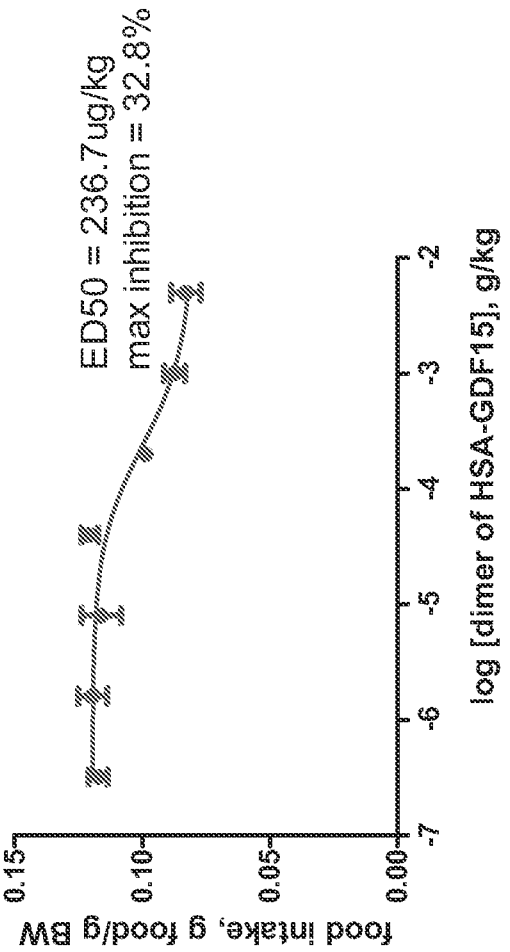

Food intake assay
Dimer of HSA-GDF15
ED50 = 236.7ug/kg
max inhibition = 32.8%
food intake, g food/g BW
0.15
0.10
0.05
0.00
-7
-6
-5
-4
-3
-2
log [dimer of HSA-GDF15], g/kg

Figure 39

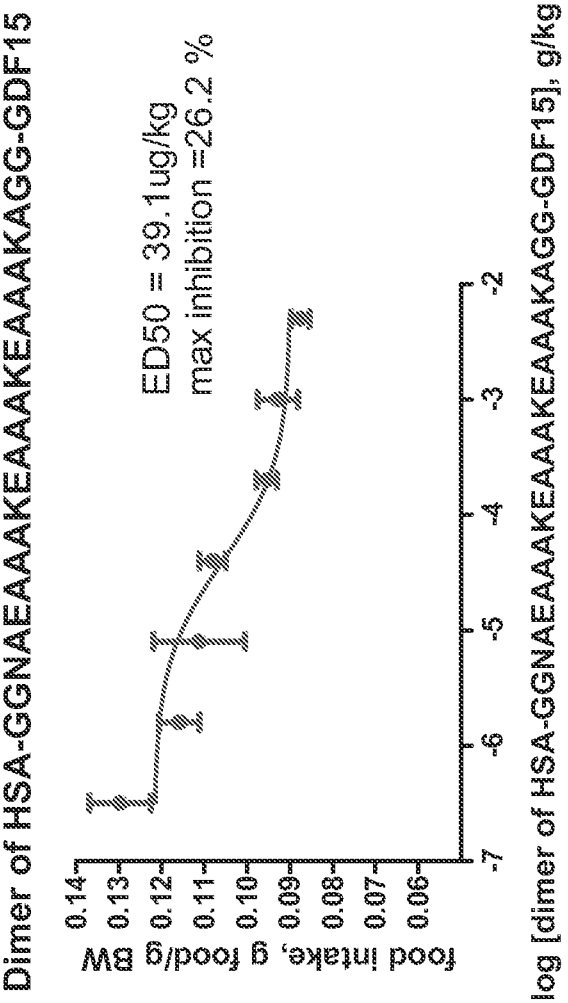

Food intake assay
Dimer of HSA-GGNAEAAAKEAAAKEAAAKAGG-GDF15
ED50 = 39.1ug/kg
max inhibition =26.2 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of HSA-GGNAEAAAKEAAAKEAAAKAGG-GDF15], g/kg

Figure 40

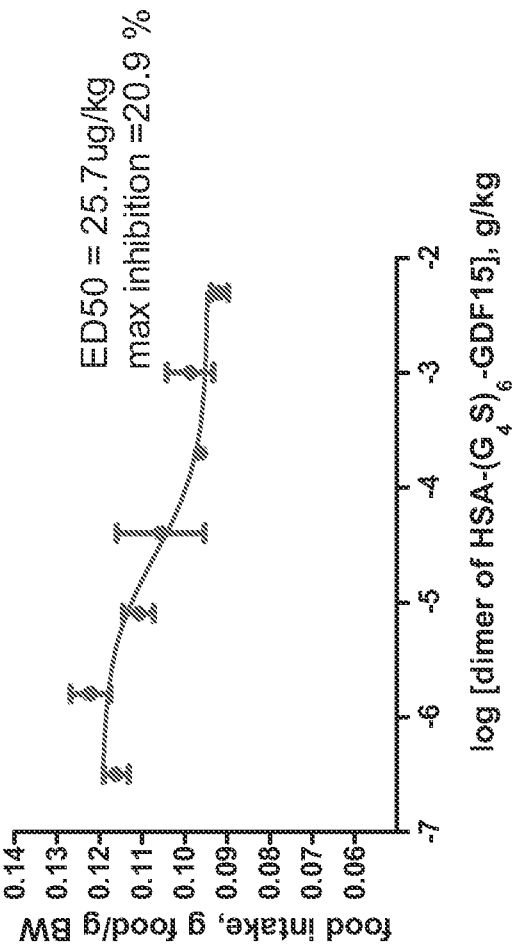

Food intake assay
Dimer of HSA-(G4S)6-GDF15
ED50 = 25.7ug/kg
max inhibition =20.9 %
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of HSA-(G4S)6-GDF15], g/kg

Figure 41

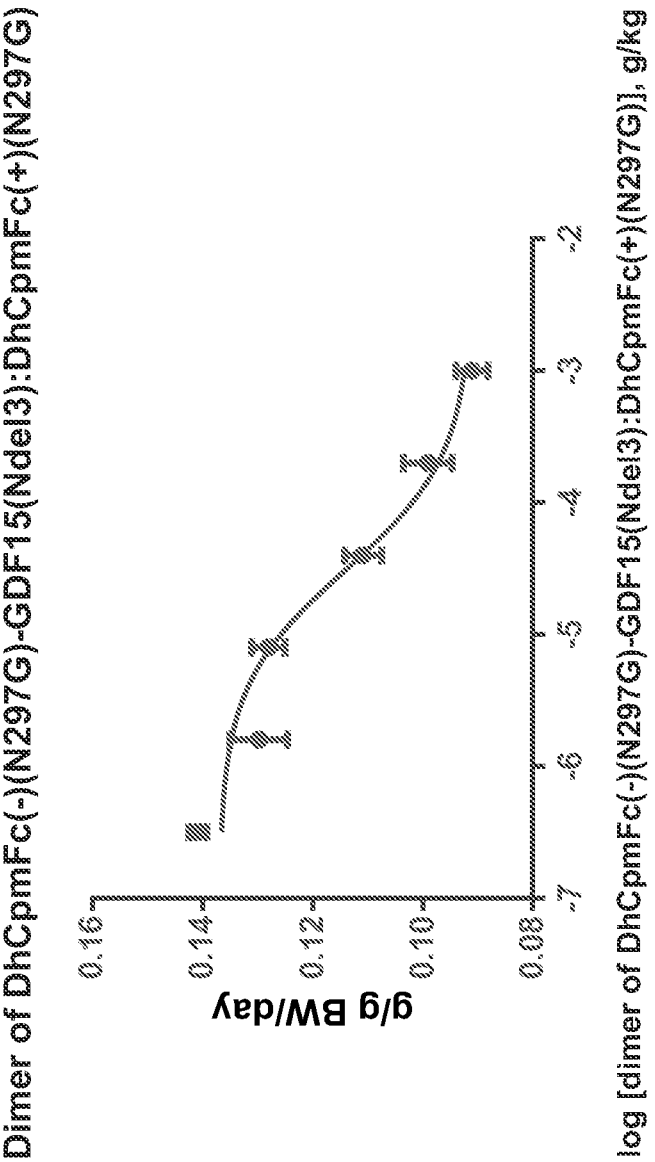

Food intake assay
Dimer of DhCpmFc(-)(N297G)-GDF15(Ndel3):DhCpmFc(+)(N297G)
g/g BW/day
0.16
0.14
0.12
0.10
0.08
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)-GDF15(Ndel3):DhCpmFc(+)(N297G)], g/kg

Figure 42

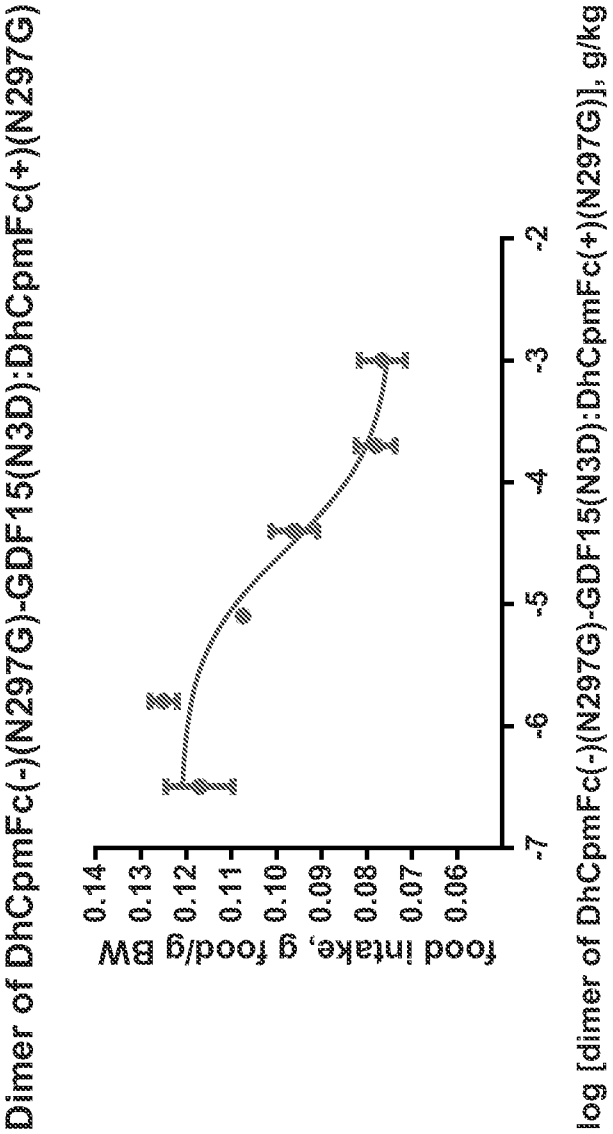

Food intake assay
Dimer of DhCpmFc(-)(N297G)-GDF15(N3D):DhCpmFc(+)(N297G)
food intake, g food/g BW
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)-GDF15(N3D):DhCpmFc(+)(N297G)], g/kg

Figure 43

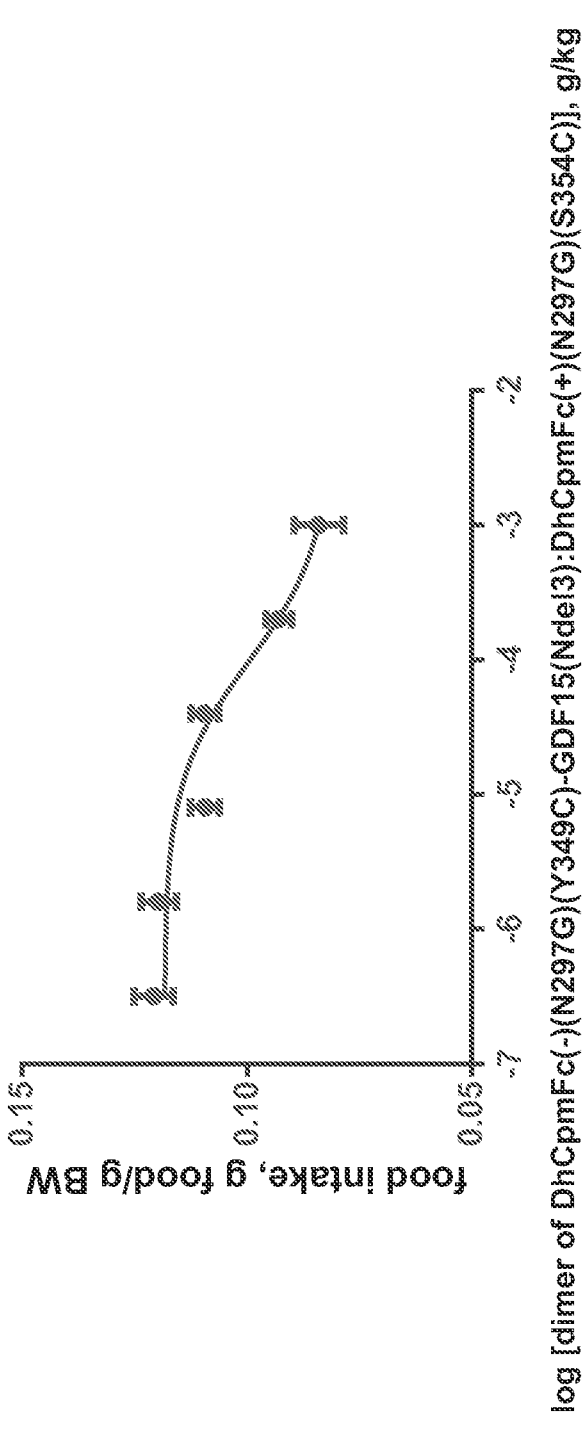

Food intake assay
Dimer of DhCpmFc(-)(N297G)(Y349C)-GDF15(Ndel3):DhCpmFc(+)(N297G)(S354C)
food intake, g food/g BW
0.15
0.10
0.05
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)(Y349C)-GDF15(Ndel3):DhCpmFc(+)(N297G)(S354C)], g/kg

Figure 44

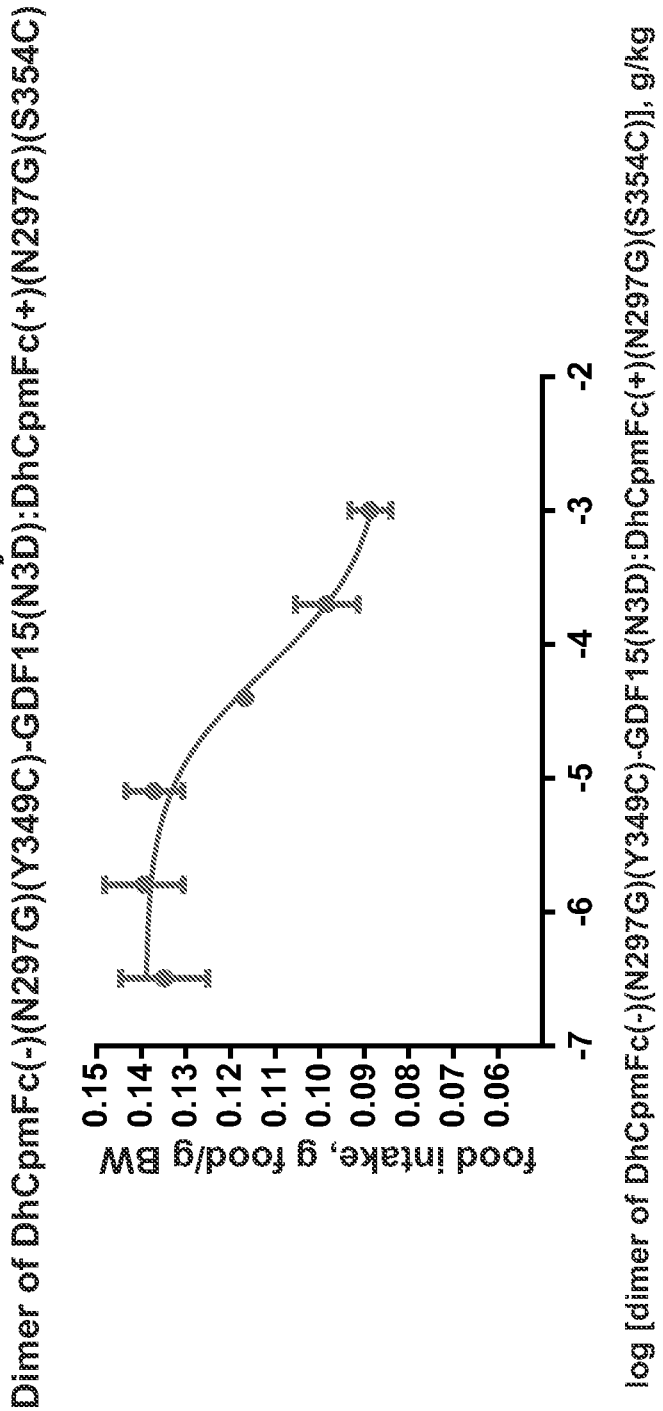

Food intake assay
Dimer of DhCpmFc(-)(N297G)(Y349C)-GDF15(N3D):DhCpmFc(+)(N297G)(S354C)
food intake, g food/g BW
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)(Y349C)-GDF15(N3D):DhCpmFc(+)(N297G)(S354C)], g/kg

Figure 45

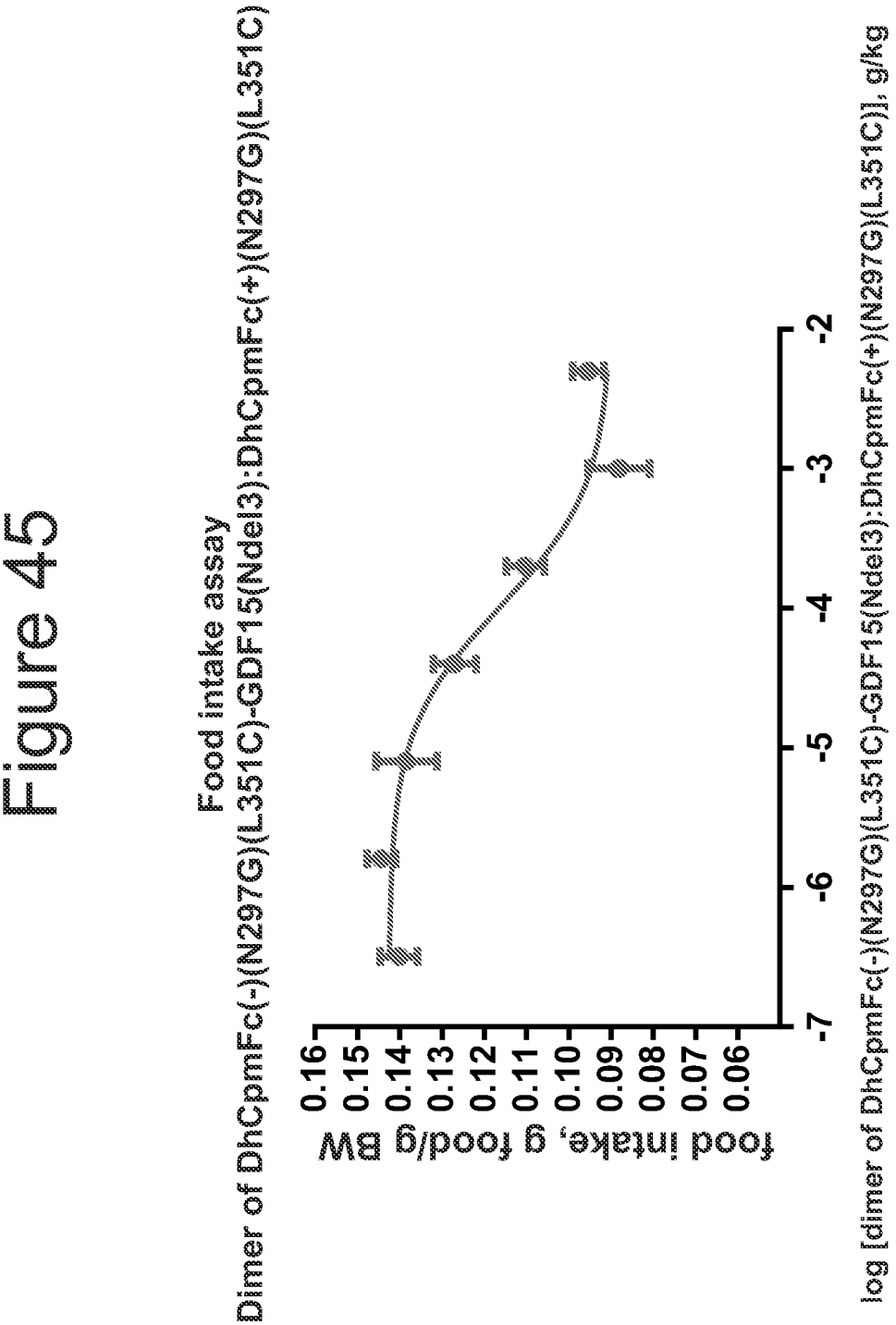

Food intake assay
Dimer of DhCpmFc(-)(N297G)(L351C)-GDF15(Ndel3):DhCpmFc(+)(N297G)(L351C)
food intake, g food/g BW
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)(L351C)-GDF15(Ndel3):DhCpmFc(+)(N297G)(L351C)], g/kg

Figure 46

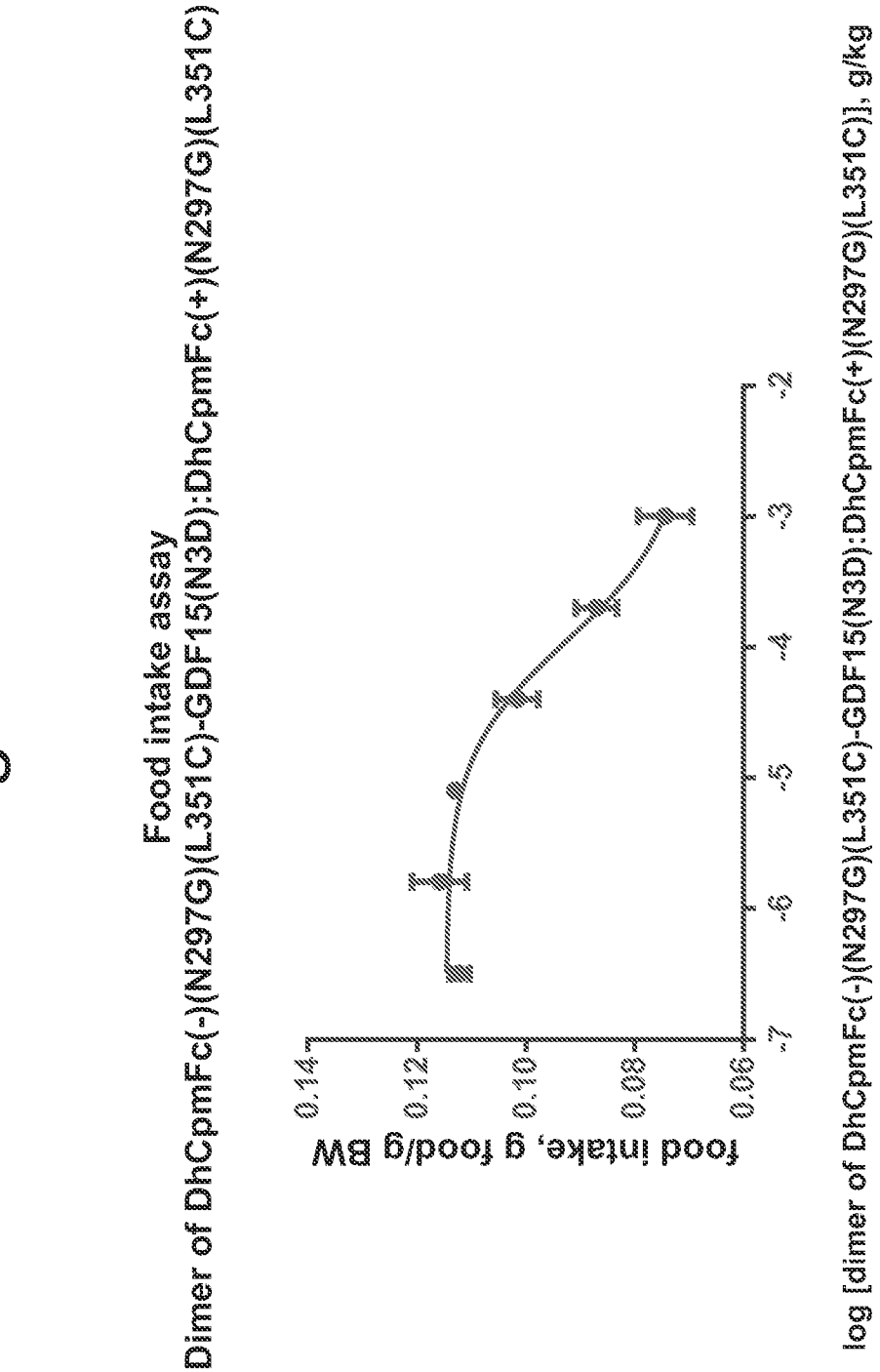

Food intake assay
Dimer of DhCpmFc(-)(N297G)(L351C)-GDF15(N3D):DhCpmFc(+)(N297G)(L351C)
food intake, g food/g BW
0.14
0.12
0.10
0.08
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)(L351C)-GDF15(N3D):DhCpmFc(+)(N297G)(L351C)], g/kg

Figure 47

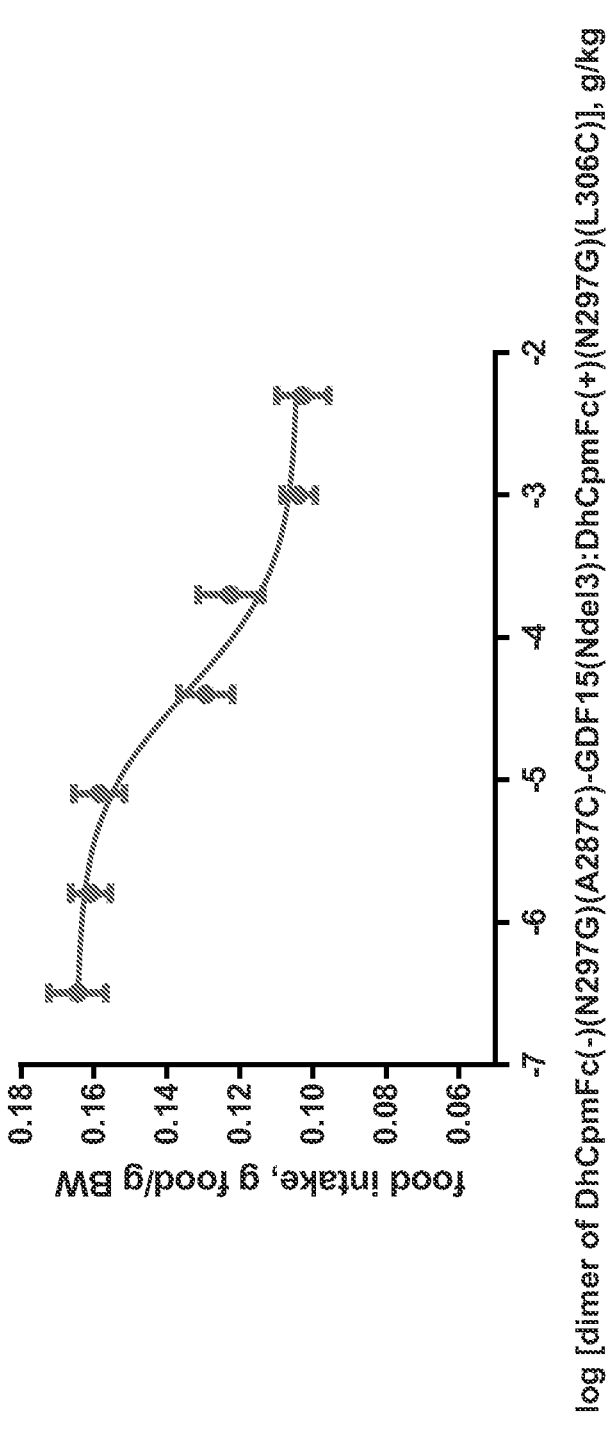

Food intake assay
Dimer of DhCpmFc(-)(N297G)(A287C)-GDF15(NdeI3):DhCpmFc(+)(N297G)(L306C)
food intake, g food/g BW
0.18
0.16
0.14
0.12
0.10
0.08
0.06
-7
-6
-5
-4
-3
-2
log [dimer of DhCpmFc(-)(N297G)(A287C)-GDF15(NdeI3):DhCpmFc(+)(N297G)(L306C)], g/kg

Figure 48

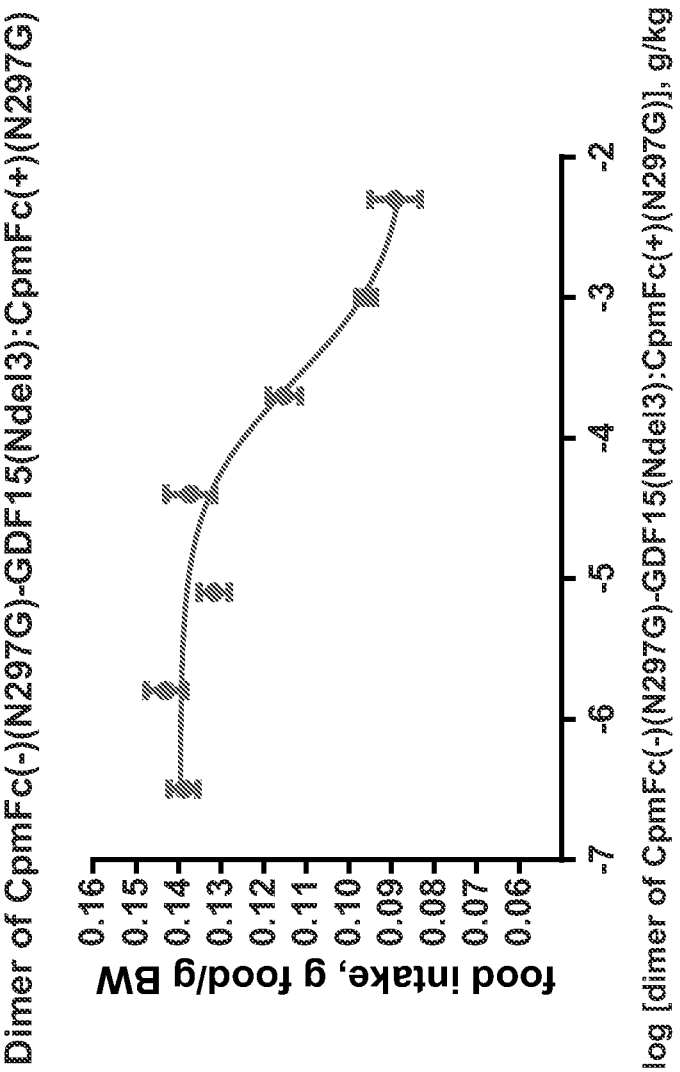

Food intake assay
Dimer of CpmFc(-)(N297G)-GDF15(Ndel3):CpmFc(+)(N297G)
food intake, g food/g BW
0.16
0.15
0.14
0.13
0.12
0.11
0.10
0.09
0.08
0.07
0.06
-7
-6
-5
-4
-3
-2
log [dimer of CpmFc(-)(N297G)-GDF15(Ndel3):CpmFc(+)(N297G)], g/kg

Figure 49

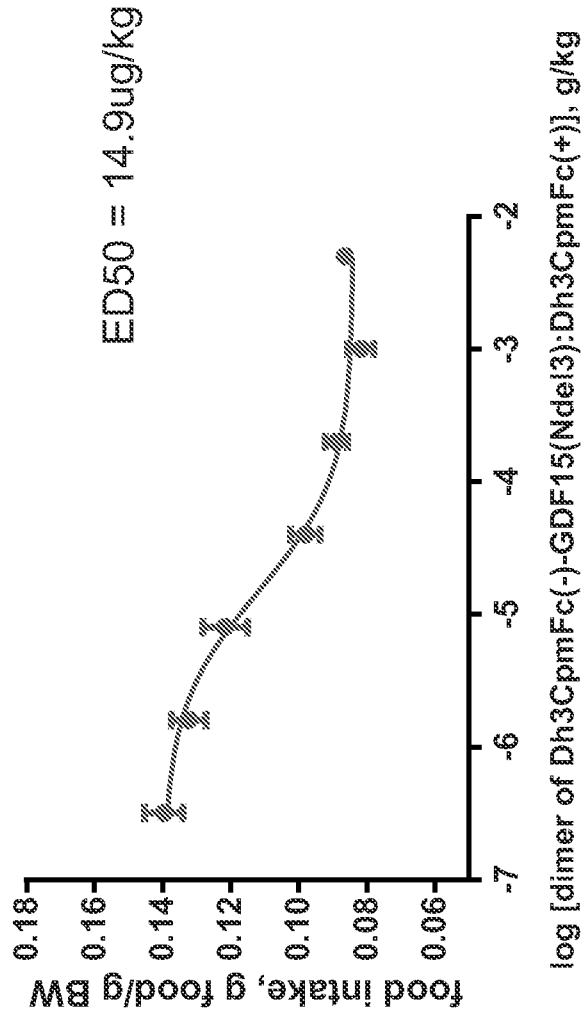

Food intake assay
Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
ED50 = 14.9ug/kg
food intake, g food/g BW
0.18
0.16
0.14
0.12
0.10
0.08
0.06
-7
-6
-5
-4
-3
-2
log [dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)], g/kg

Figure 50

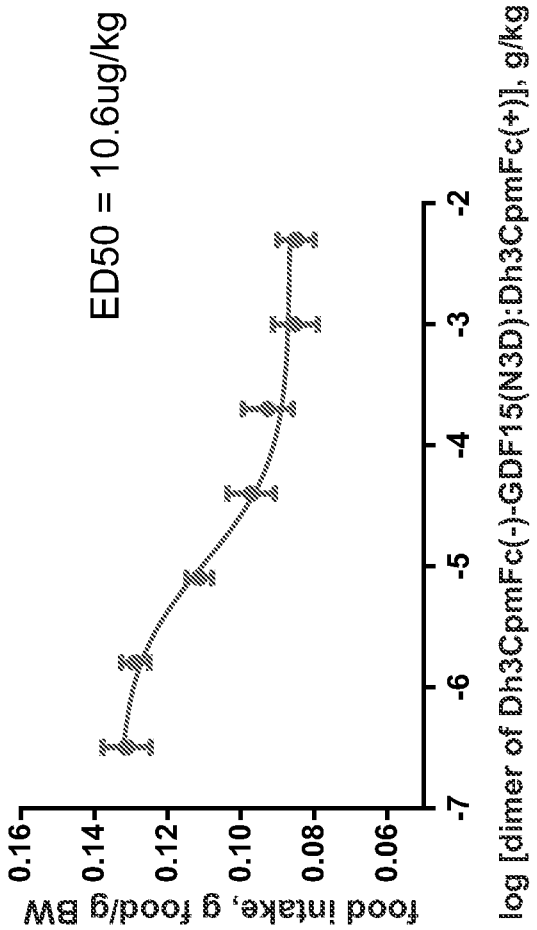

Food intake assay
Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
ED50 = 10.6ug/kg
food intake, g food/g BW
0.16
0.14
0.12
0.10
0.08
0.06
-7
-6
-5
-4
-3
-2
log [dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)], g/kg

Figure 51

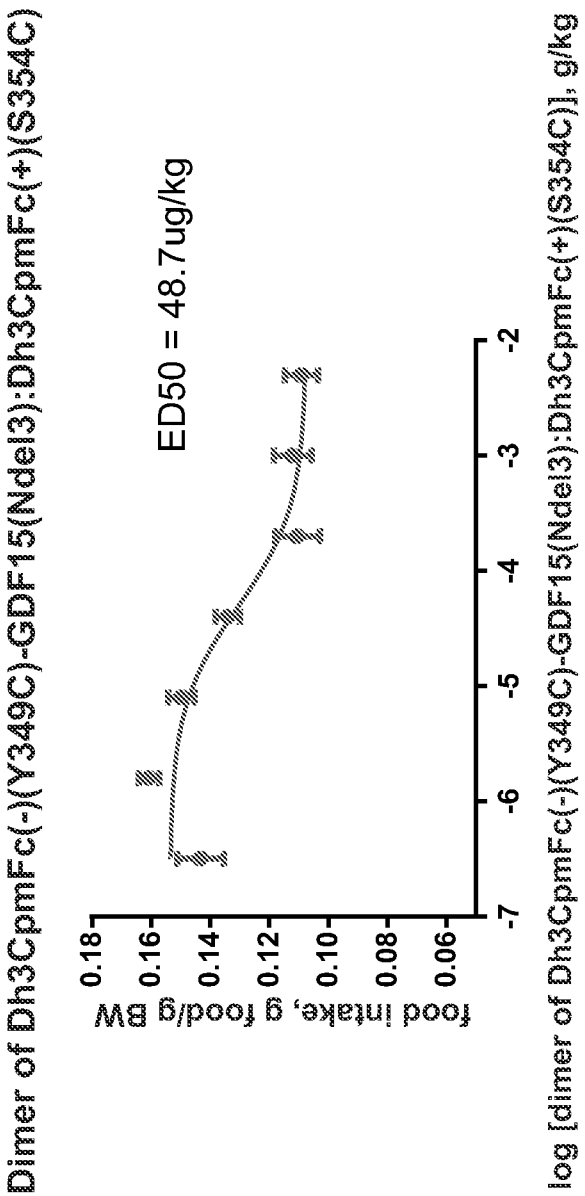

Food intake assay
Dimer of Dh3CpmFc(-)(Y349C)-GDF15(Ndel3):Dh3CpmFc(+)(S354C)
ED50 = 48.7ug/kg
food intake, g food/g BW
0.18
0.16
0.14
0.12
0.10
0.08
0.06
-7
-6
-5
-4
-3
-2
log [dimer of Dh3CpmFc(-)(Y349C)-GDF15(Ndel3):Dh3CpmFc(+)(S354C)], g/kg

Figure 52

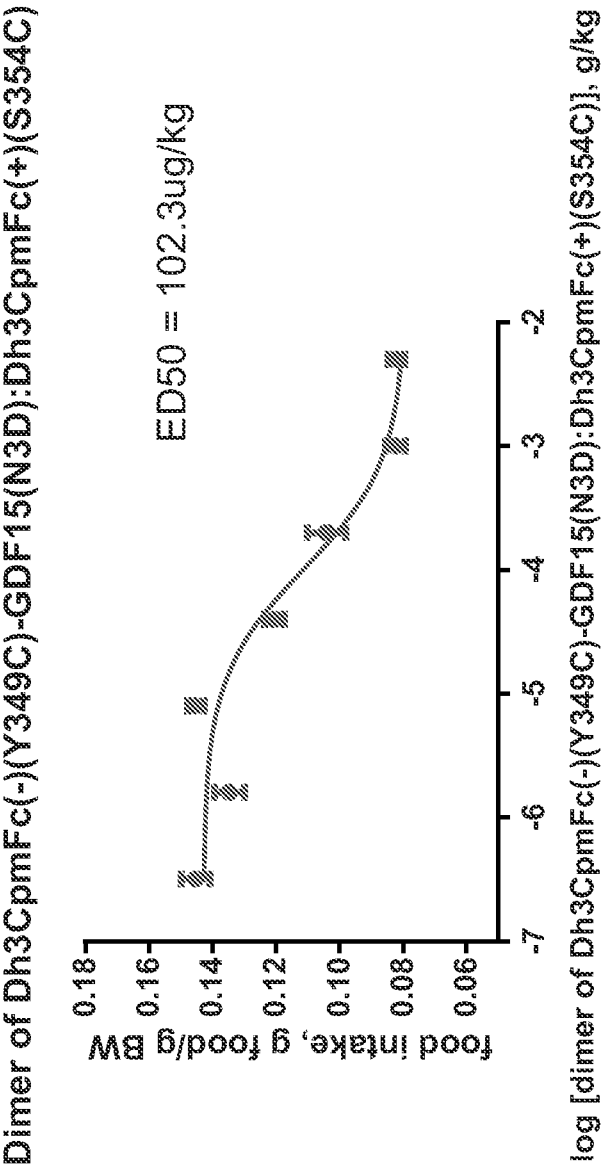

Food intake assay
Dimer of Dh3CpmFc(-)(Y349C)-GDF15(N3D):Dh3CpmFc(+)(S354C)
ED50 = 102.3ug/kg
food intake, g food/g BW
0.18
0.16
0.14
0.12
0.10
0.08
0.06
-7
-6
-5
-4
-3
-2
log [dimer of Dh3CpmFc(-)(Y349C)-GDF15(N3D):Dh3CpmFc(+)(S354C)], g/kg

Figure 53

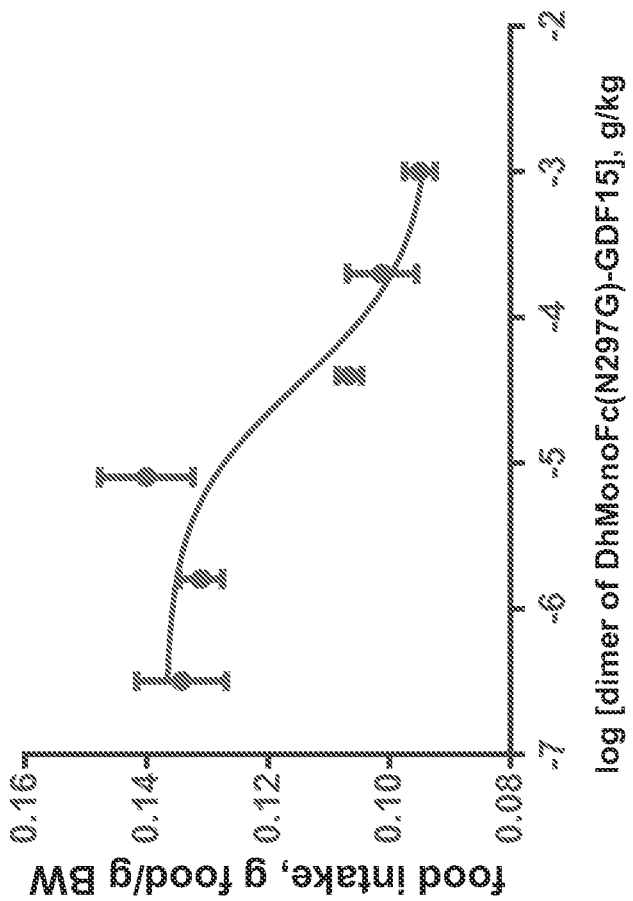

Food intake assay
Dimer of DhMonoFc(N297G)-GDF15
food intake, g food/g BW
0.16
0.14
0.12
0.10
0.08
-7
-6
-5
-4
-3
-2
log [dimer of DhMonoFc(N297G)-GDF15], g/kg

Figure 54

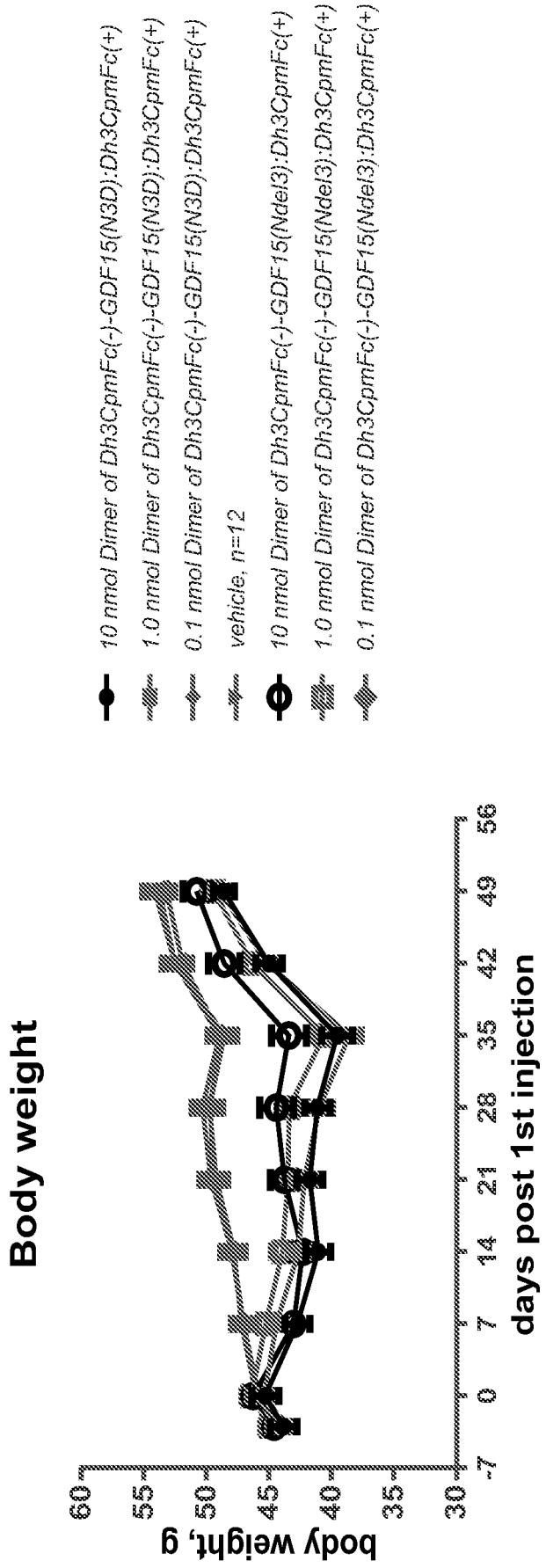

Body weight
body weight, g
60
55
50
45
40
35
30
-7
0
7
14
21
28
35
42
49
56
days post 1st injection
10 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
vehicle, n=12
10 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)

Figure 55

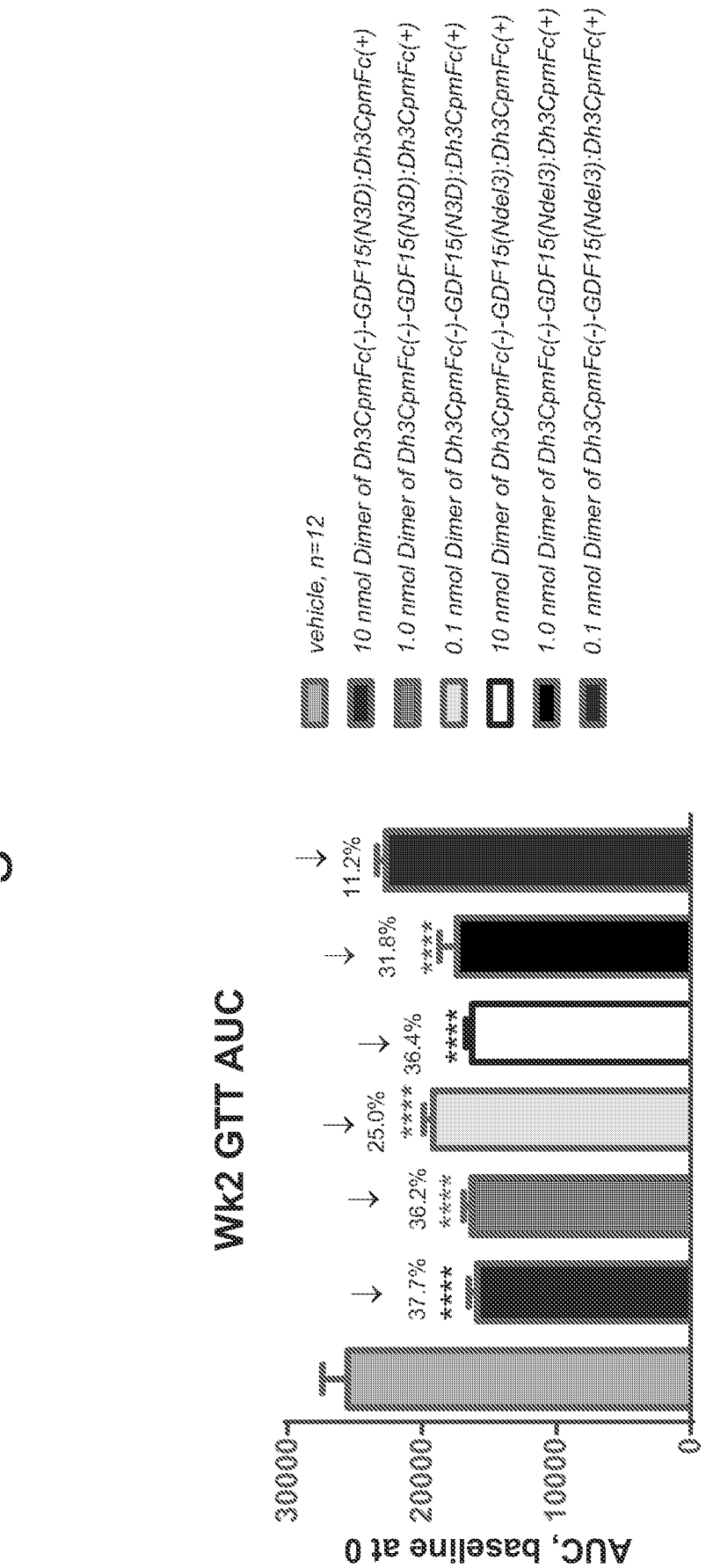

Wk2 GTT AUC
AUC, baseline at 0
30000
20000
10000
0
37.7%
****
36.2%
****
25.0%
****
36.4%
****
31.8%
****
11.2%
vehicle, n=12
10 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
10 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)

Figure 56

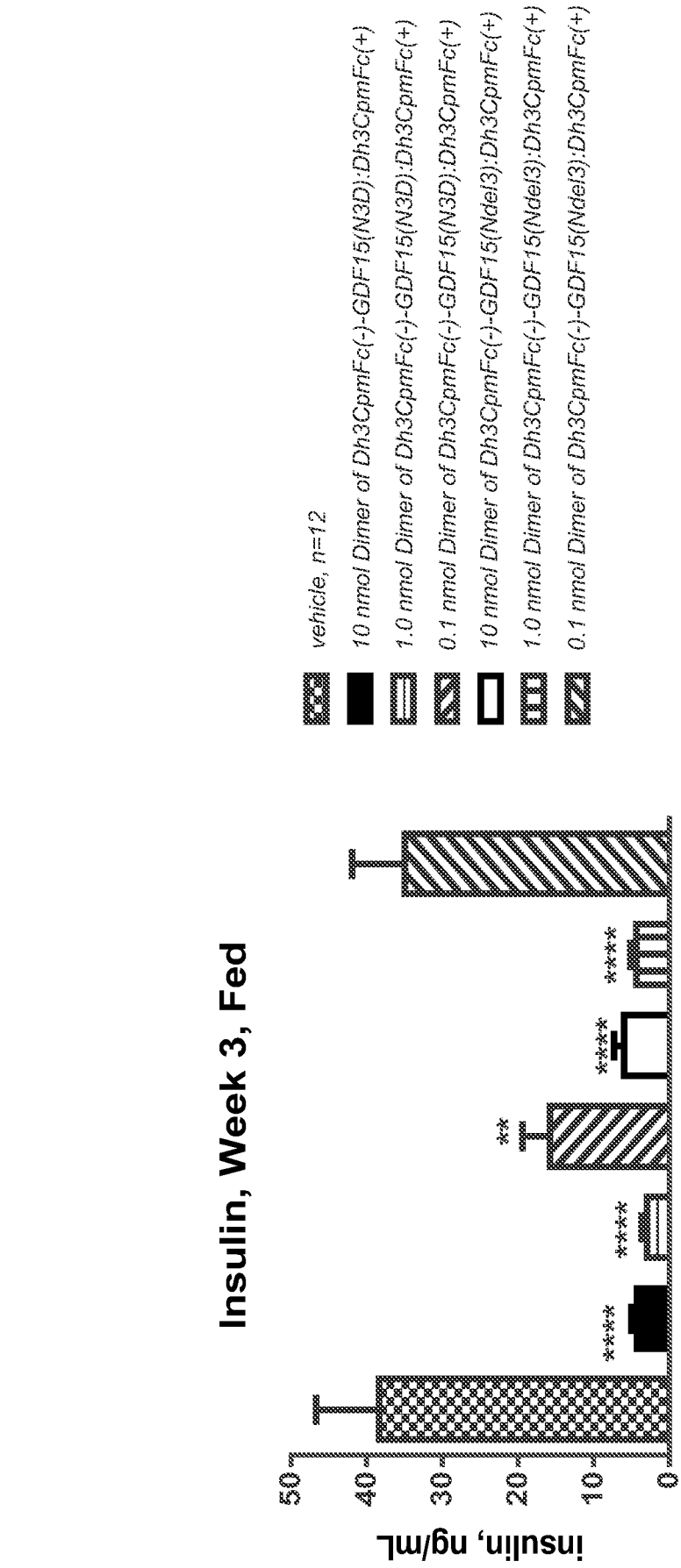

Insulin, Week 3, Fed
insulin, ng/mL
0
10
20
30
40
50
****
****
**
****
****
vehicle, n=12
10 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
10 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)

Figure 57

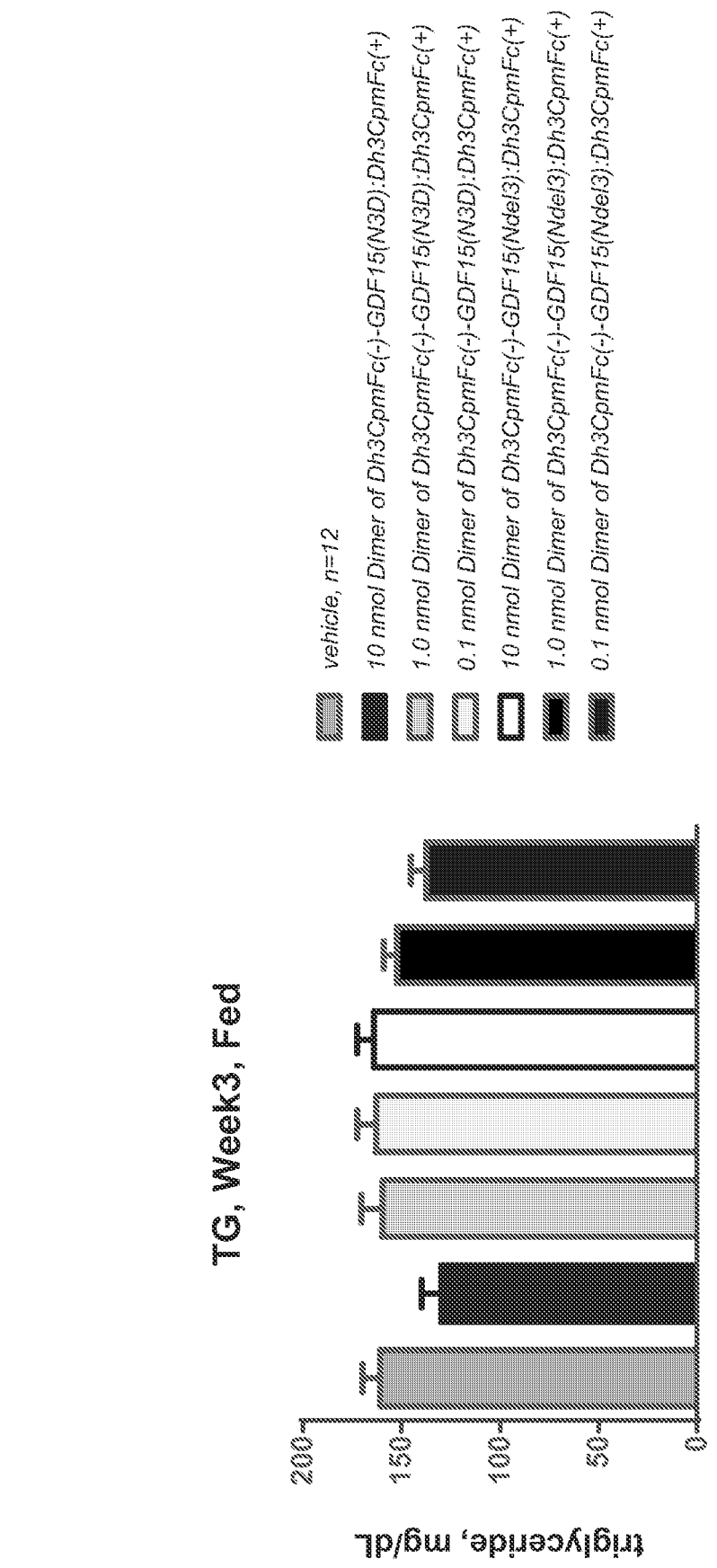

TG, Week3, Fed
triglyceride, mg/dL
200
150
100
50
0
vehicle, n=12
10 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
10 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)

Figure 58

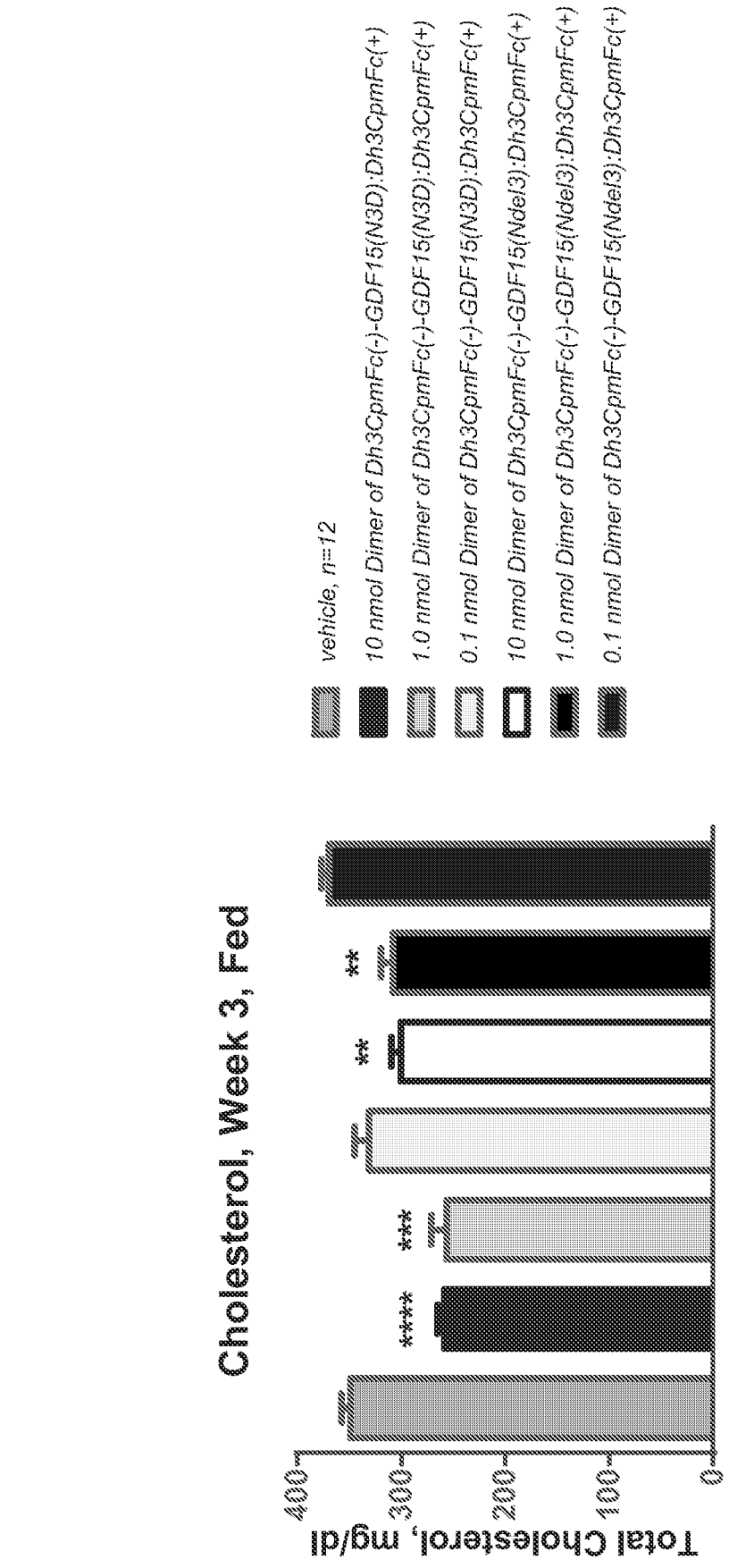

Cholesterol, Week 3, Fed
Total Cholesterol, mg/dl
0
100
200
300
400
****
***
**
**
vehicle, n=12
10 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
10 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)

Figure 59

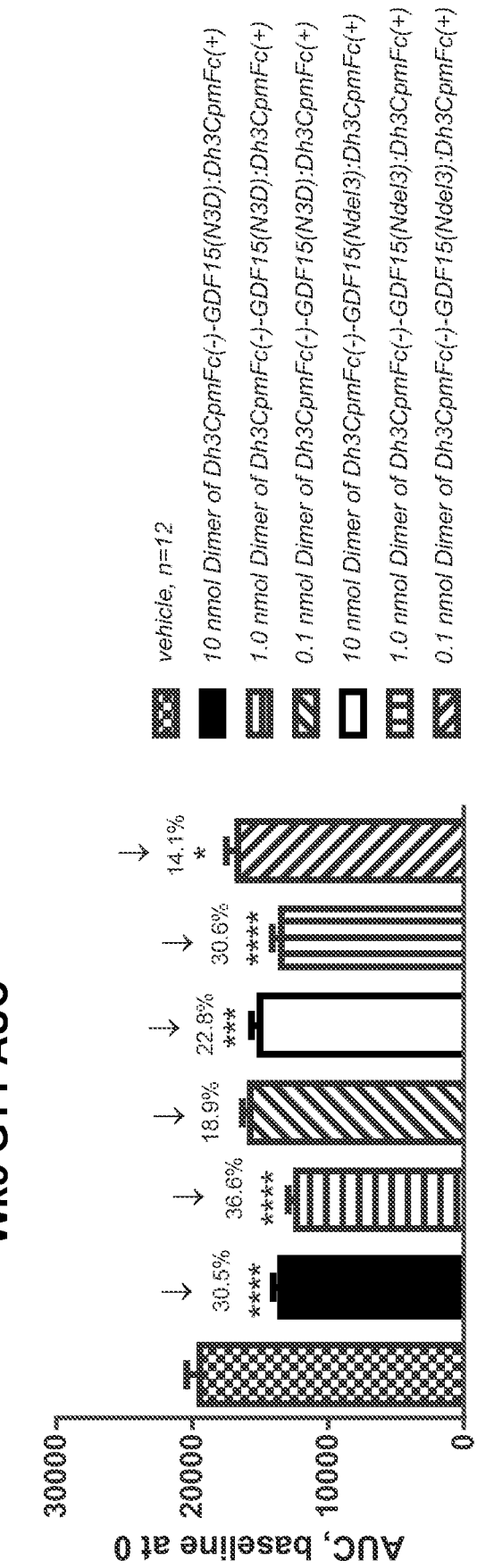

Wk5 GTT AUC
AUC, baseline at 0
30000
20000
10000
0
30.5%
****
36.6%
****
18.9%
22.8%
***
30.6%
****
14.1%
*
vehicle, n=12
10 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
10 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
1.0 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
0.1 nmol Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)

Figure 60

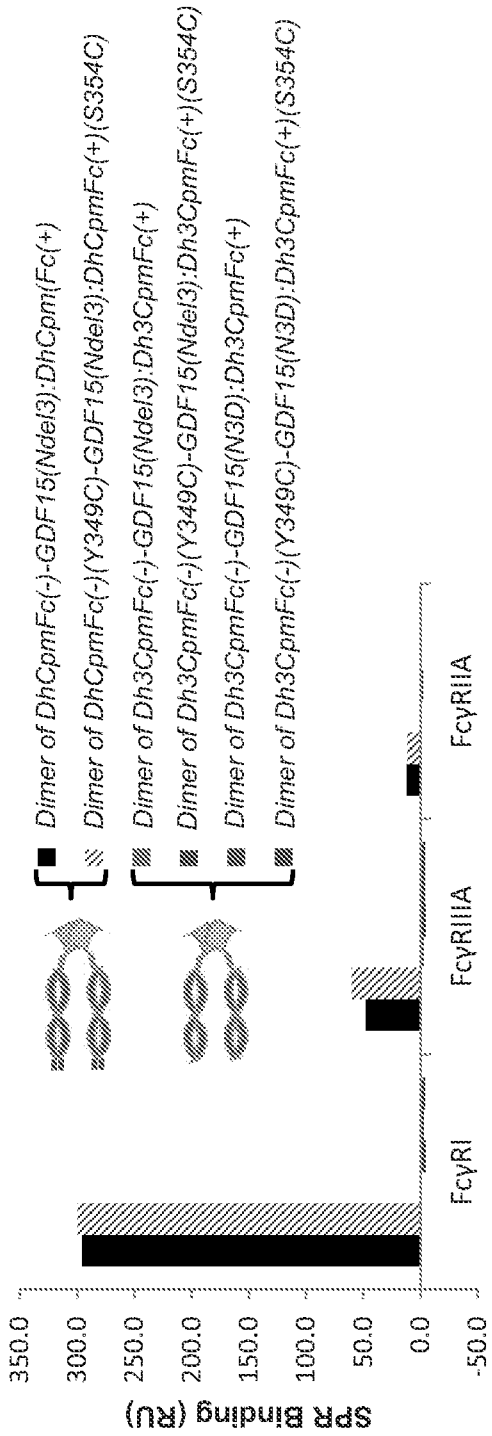
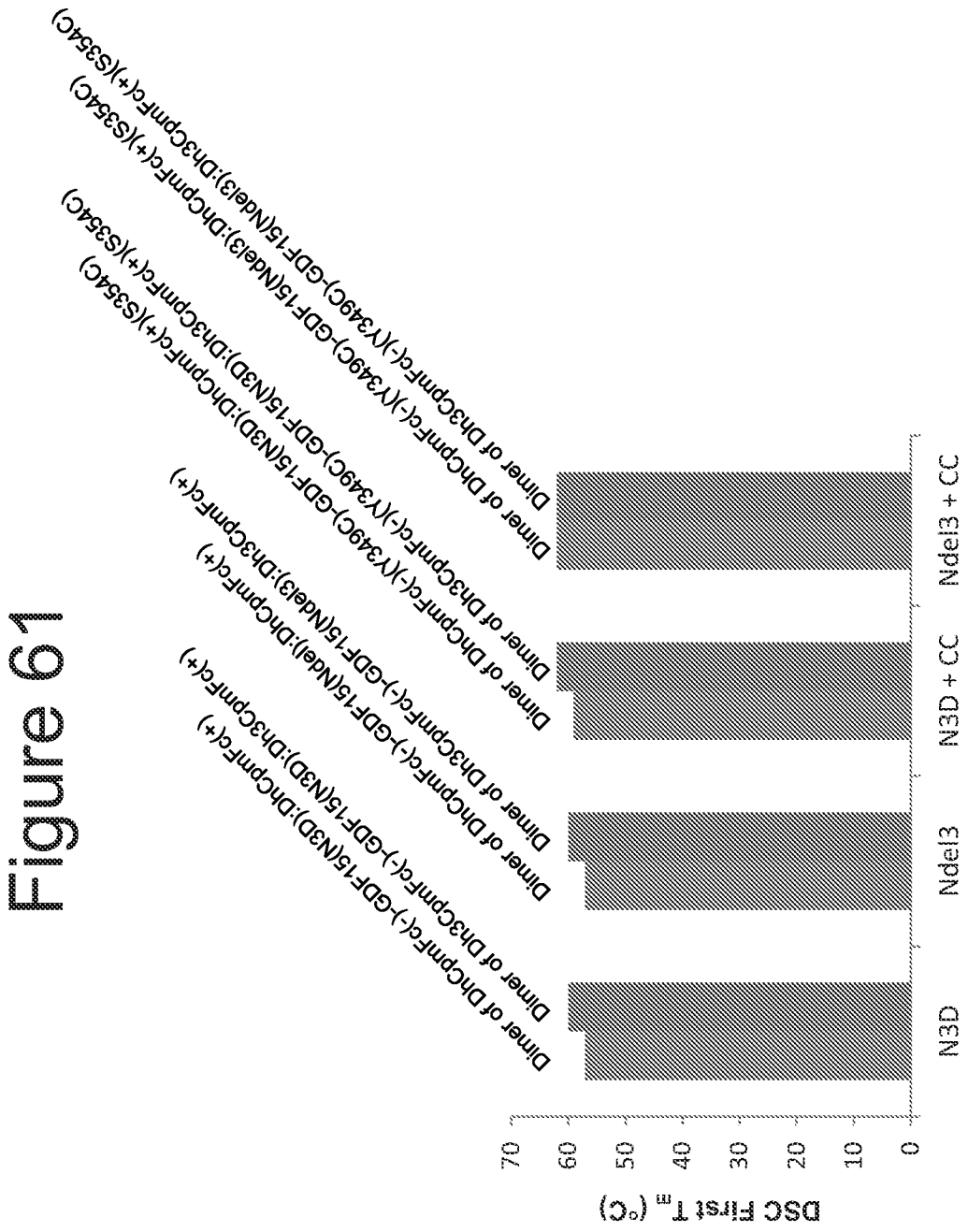

Dimer of DhCpmFc(-)-GDF15(Ndel3):DhCpm(Fc(+)
Dimer of DhCpmFc(-)(Y349C)-GDF15(Ndel3):DhCpmFc(+)(S354C)
Dimer of Dh3CpmFc(-)-GDF15(Ndel3):Dh3CpmFc(+)
Dimer of Dh3CpmFc(-)(Y349C)-GDF15(Ndel3):Dh3CpmFc(+)(S354C)
Dimer of Dh3CpmFc(-)-GDF15(N3D):Dh3CpmFc(+)
Dimer of Dh3CpmFc(-)(Y349C)-GDF15(N3D):Dh3CpmFc(+)(S354C)
SPR binding (RU)
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
-50.0
FcγRI
FcγRIIIA
FcγRIIA

Figure 61


DSC First T_m (°C)
0
10
20
30
40
50
60
70
N3D
Ndel3
N3D + CC
Ndel3 + CC
Dimer of DhCpmFc(-)-GDF-15(N3D):DhCpmFc(+)
Dimer of DhCpmFc(-)-GDF-15(Ndel):DhCpmFc(+)
Dimer of DhCpmFc(-)(Y349C)-GDF-15(N3D):DhCpmFc(+)(S354C)
Dimer of DhCpmFc(-)(Y349C)-GDF-15(Ndel3):DhCpmFc(+)(S354C)