Figure 1

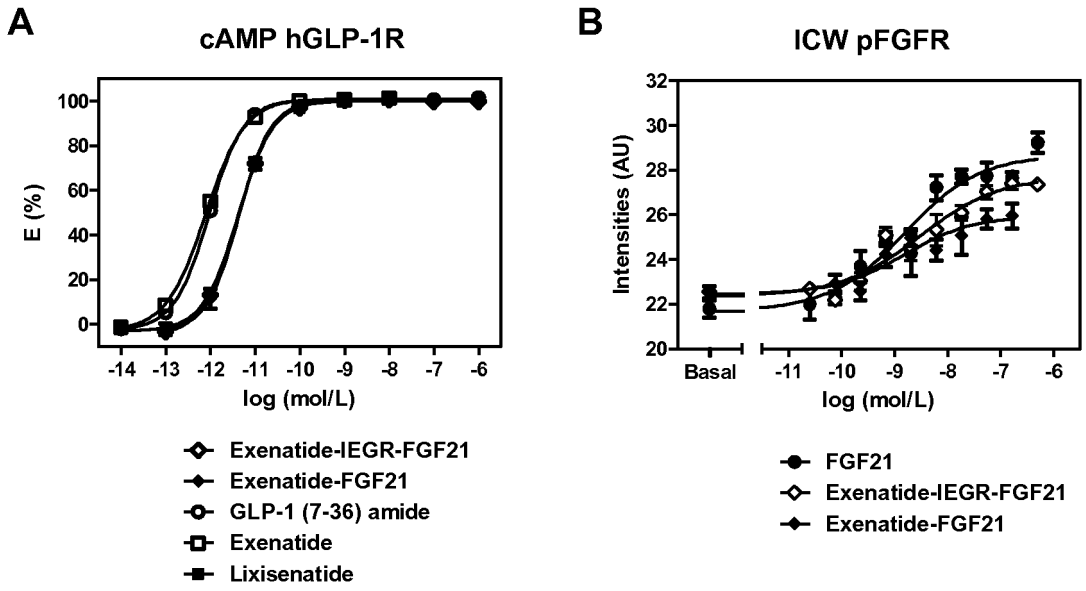

A
cAMP hGLP-1R
E (%)
100
80
60
40
20
0
-14 -13 -12 -11 -10 -9 -8 -7 -6
log (mol/L)
Exenatide-IEGR-FGF21
Exenatide-FGF21
GLP-1 (7-36) amide
Exenatide
Lixisenatide
B
ICW pFGFR
Intensities (AU)
32
30
28
26
24
22
20
Basal -11 -10 -9 -8 -7 -6
log (mol/L)
FGF21
Exenatide-IEGR-FGF21
Exenatide-FGF21

Figure 1 (continued)

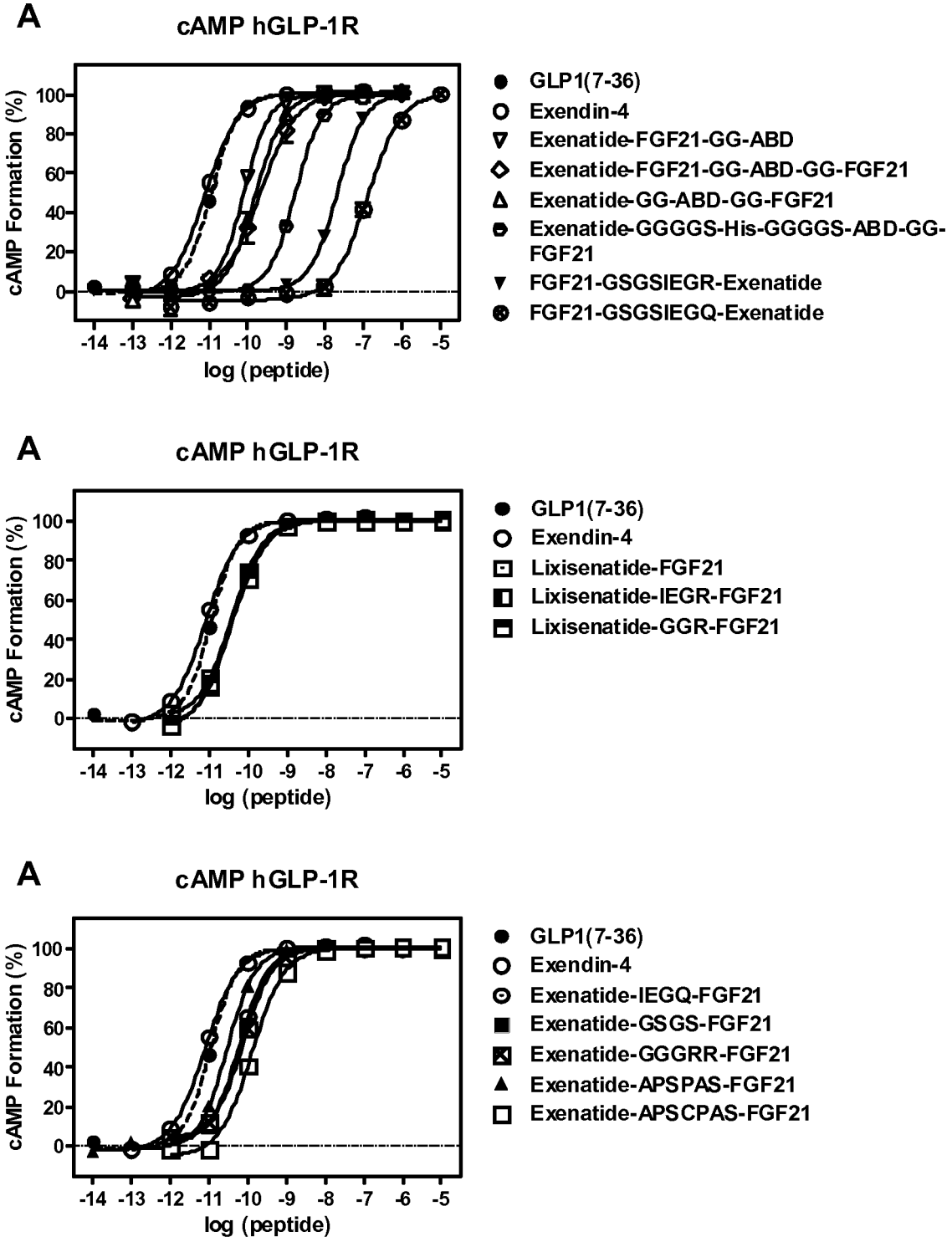


Figure 1 (continued)

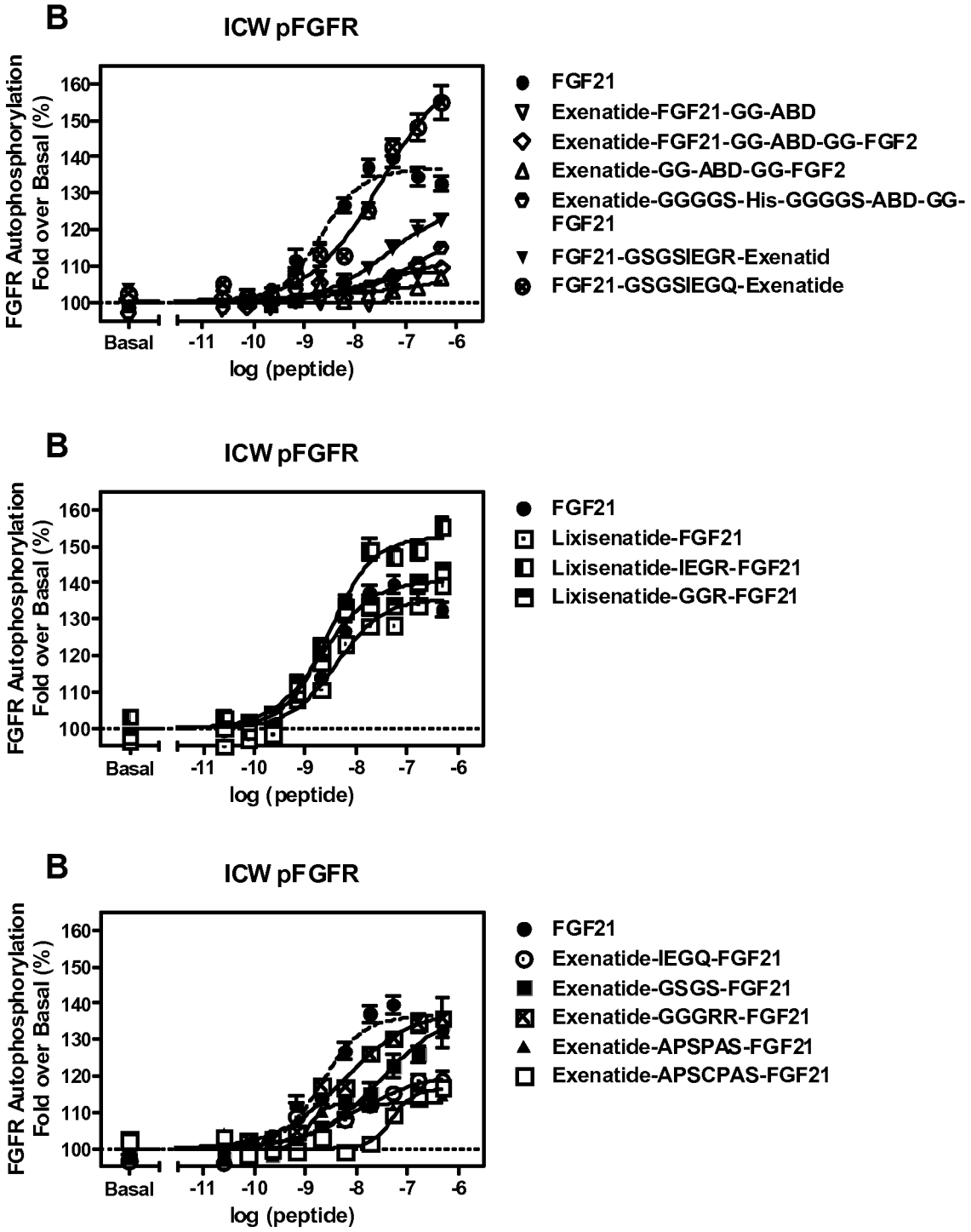


Figure 1 (continued)

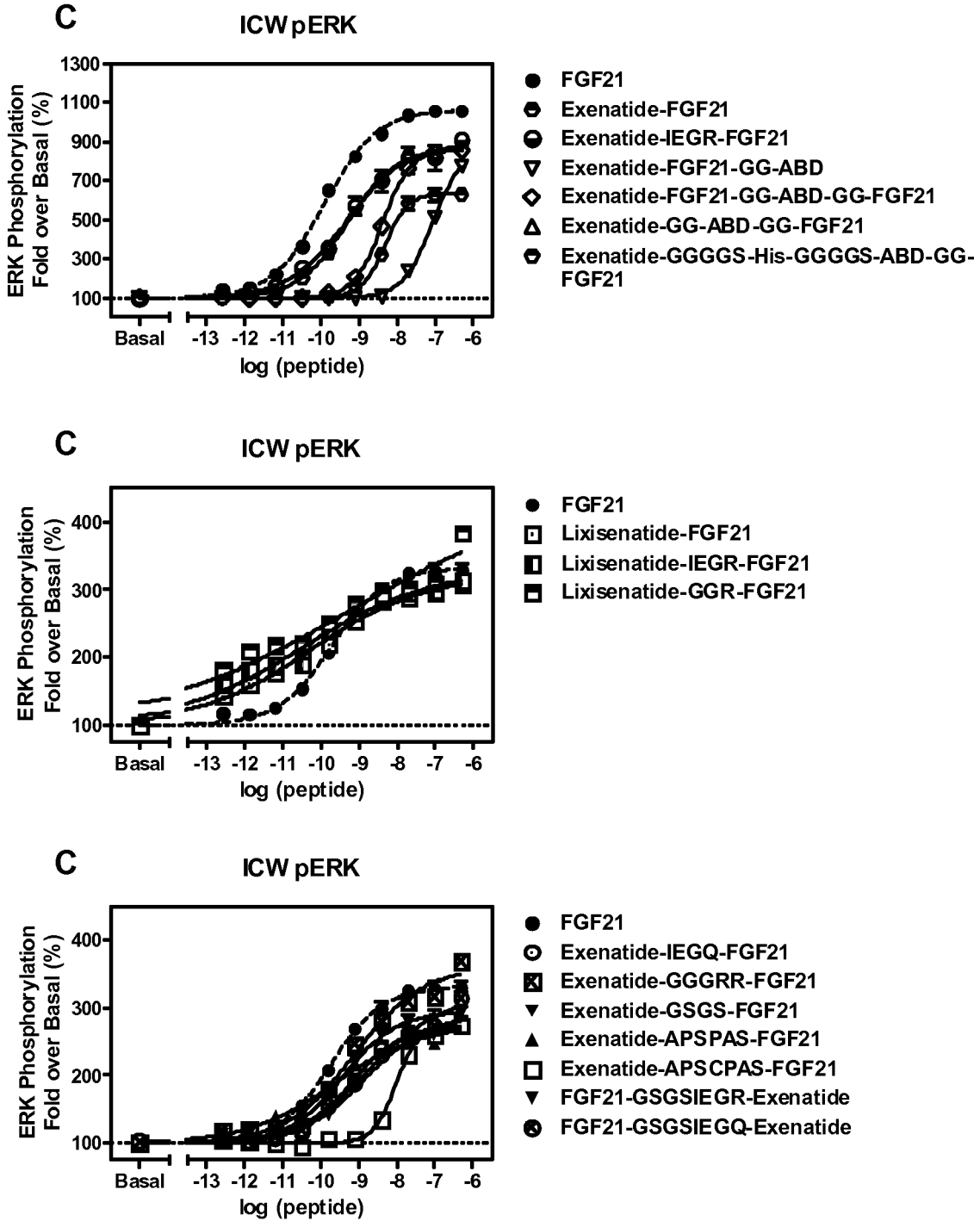


Figure 2

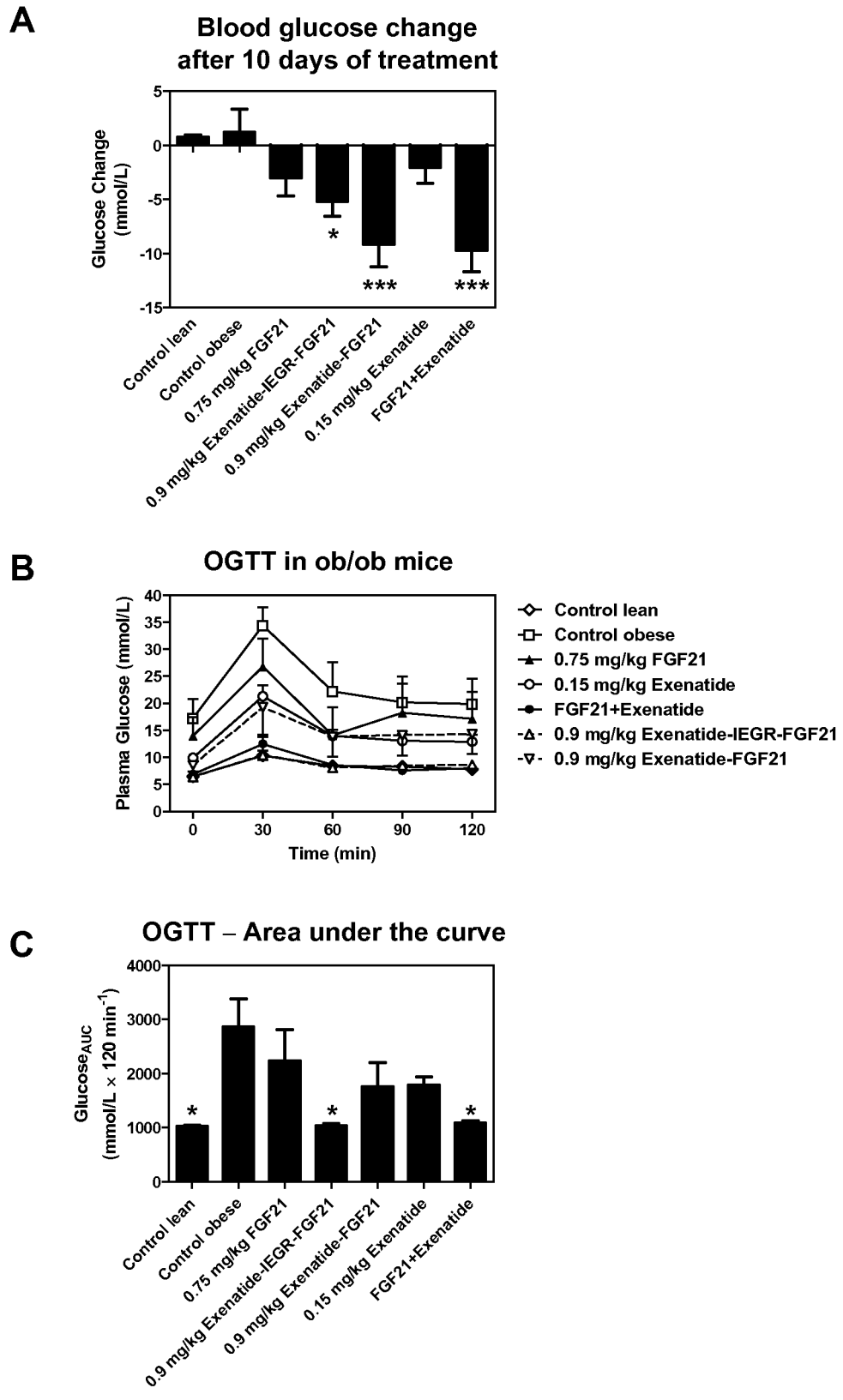

A
Blood glucose change after 10 days of treatment
Glucose Change (mmol/L)
5
0
-5
-10
-15
*
***
***
Control lean
Control obese
0.75 mg/kg FGF21
0.9 mg/kg Exenatide-IEGR-FGF21
0.9 mg/kg Exenatide-FGF21
0.15 mg/kg Exenatide
FGF21+Exenatide
B
OGTT in ob/ob mice
Plasma Glucose (mmol/L)
40
35
30
25
20
15
10
5
0
0
30
60
90
120
Time (min)
Control lean
Control obese
0.75 mg/kg FGF21
0.15 mg/kg Exenatide
FGF21+Exenatide
0.9 mg/kg Exenatide-IEGR-FGF21
0.9 mg/kg Exenatide-FGF21
C
OGTT – Area under the curve
GlucoseAUC (mmol/L × 120 min-1)
4000
3000
2000
1000
0
*
*
*
Control lean
Control obese
0.75 mg/kg FGF21
0.9 mg/kg Exenatide-IEGR-FGF21
0.9 mg/kg Exenatide-FGF21
0.15 mg/kg Exenatide
FGF21+Exenatide

Figure 3

a) FGF-21 compounds

Human FGF-21 – including signal sequence (Native Human FGF-21 – including signal sequence)
(signal sequence is bold and underlined)
MDSDETGFEHSGLWVSVLAGLLLGACQAHPIPDSSPLLQPGGQVRQRYLYTDDAQQTEAHLEIREDGT
VGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQ
SEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRS
PSYAS

(SEQ ID NO: 1)

FGF-21 mutein (G + Native Human FGF-21 – including signal sequence)

GMDSDETGFE HSGLWVSVLA GLLLGACQAH PIPDSSPLLQ PGGQVRQRYL YTDDAQQTEA
HLEIREDGTV GGAADQSPES LLQLKALKPG VIQILGVKTS RFLCQRPDGA LYGSLHFDPE
ACSFRELLLE DGYNVYQSEA HGLPLHLPGN KSPHRDPAPR GPARFLPLPG LPPAPPEPPG
ILAPQPPDVG SSDPLSMVGP SQGRSPSYAS

(SEQ ID NO: 2)

FGF-21 H29-S209 / Mature FGF-21 (Native Human FGF-21 without signal sequence)

HPIPDSSPLLQPGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKT
SRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLP
GLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 3)

b) GLP1-agonists

Exenatide
HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPPS-NH_2

(SEQ ID NO: 4)

Human GLP-1(7-37)
HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG

(SEQ ID NO: 5)

Oxyntomodulin
HSQGTFTSDYSKYLDSRRAQDFVQWLMNTKRNRNNIA

(SEQ ID NO: 6)

Human GLP-1(7-36)NH_2
HAEGTFTSDVSSYLEGQAAKEFIAWLVKGR-NH_2

(SEQ ID NO: 7)

Exendin-4
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS-NH_2

(SEQ ID NO: 8)

Lixisenatide
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK-NH2
(SEQ ID NO: 9)

Lixisenatide
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK-NH2
(SEQ ID NO: 10)

FGF-21 mutein (G + FGF-21 without signal sequence)
GHPIPDSSPLLQ PGGQVRQRYL YTDDAQQTEA HLEIREDGTV GGAADQSPES LLQLKALKPG VIQILGVKTS RFLCQRPDGA LYGSLHFDPE ACSFRELLLE DGYNVYQSEA HGLPLHLPGN KSPHRDPAPR GPARFLPLPG LPPAPPEPPG ILAPQPPDVG SSDPLSMVGP SQGRSPSYAS
(SEQ ID NO: 102)

c) functional moieties for constructing the linker

Factor Xa cleavage site
IEGR
(SEQ ID NO: 11)

Pasylation unit sequence
APASPAS
(SEQ ID NO: 12)

Pasylation sequence with site for covalent modification (C)
APASCPAS
(SEQ ID NO: 13)

Protease cleavage site
GGGRR
(SEQ ID NO: 14)

Fc fragment 1: IgG 1 Asp103-Lys329
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK GFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP GK
(SEQ ID NO: 79)

Fc fragment 2: IgG1 Pro120-Lys329
PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 80)

Fc fragment 3: IgG1 Pro120-Lys329 mutated
PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT**S**PPSRDELTKNQVSL**R**C**H**VKGFYPSDIAVEWESNGQP ENNYKTT**K**PVLDSDGSF**E**L**K**S**A**LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 81)

Fc fragment 4: IgG1 Pro120-Lys222
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAK
(SEQ ID NO: 82)

GG-(IgG 1 Asp103-Lys329)-GG
GGDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPRE
EQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGKGG
(SEQ ID NO: 83)

GG-(IgG1 Pro120-Lys329)-GG
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGG
(SEQ ID NO: 84)

GG-(IgG1 Pro120-Lys329 mutated)-GG
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYT**S**PPSRDELTKNQVSL**R**C**H**VKGFYPSDIAVEWESNG
QPENNYKTT**K**PVLDSDGSF**E**L**K**S**A**LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGG
(SEQ ID NO: 85)

GG-(IgG1 Pro120-Lys222)-GG
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGG
(SEQ ID NO: 86)

Albumin-Binding Domain (ABD)
LAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALP
(SEQ ID NO: 87)

GG-Albumin-Binding Domain-GG
(GG-ABD-GG = linker)
GGLAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALPGG
(SEQ ID NO: 88)

GGGGS-Albumin-Binding Domain-GGGGS
(GGGGS-ABD-GGGGS = linker)
GGGGSLAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALPGGGGS
(SEQ ID NO: 89)

Human Serum Albumine (HSA)
DAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVADESAENCDKSLHTLFGDKLC
TVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNEETFLKKYLYEIARRHPYFY
APELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKFGERAFKAWAVARLSQRFPK
AEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDEMPA
DLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETTLEKCCAAADPHECYAKVFD
EFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLGKVGSKCCKHPEAKRMPCAE
DYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKK
QTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQAALGL
(SEQ ID NO: 90)

Human Serum Albumine (HSA) with linker (GG[GGGGS]$_3$)A-HSA-GG[GGGGS]$_3$)A)
GGGGGGGSGGGGSGGGGSADAHKSEVAHRFKDLGEENFKALVLIAFAQYLQQCPFEDHVKLVNEVTEFAKTCVAD
ESAENCDKSLHTLFGDKLCTVATLRETYGEMADCCAKQEPERNECFLQHKDDNPNLPRLVRPEVDVMCTAFHDNE
ETFLKKYLYEIARRHPYFYAPELLFFAKRYKAAFTECCQAADKAACLLPKLDELRDEGKASSAKQRLKCASLQKF
GERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTKVHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEK
PLLEKSHCIAEVENDEMPADLPSLAADFVESKDVCKNYAEAKDVFLGMFLYEYARRHPDYSVVLLLRLAKTYETT
LEKCCAAADPHECYAKVFDEFKPLVEEPQNLIKQNCELFEQLGEYKFQNALLVRYTKKVPQVSTPTLVEVSRNLG
KVGSKCCKHPEAKRMPCAEDYLSVVLNQLCVLHEKTPVSDRVTKCCTESLVNRRPCFSALEVDETYVPKEFNAET
FTFHADICTLSEKERQIKKQTALVELVKHKPKATKEQLKAVMDDFAAFVEKCCKADDKETCFAEEGKKLVAASQA
ALGLGGGGGGGSGGGGSGGGGSA
(SEQ ID NO: 91)

Sequence with multiple His-residues 1
HAHGHGHAHGGGGS
(SEQ ID NO: 92)

Sequence with multiple His-residues 2
HAHGHGHAH
(SEQ ID NO: 93)

FGF21 (without signal sequence) based linker
HPIPDSSPLLQPGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKT
SRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLP
GLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS
(SEQ ID NO: 94)

PASylation Sequence 1
ASPAAPAPASPAAPAPSAPA (SEQ ID NO: 95)

PASylation Sequence 2
AAPASPAPAAPSAPAPAAPS (SEQ ID NO: 96)

PASylation Sequence 3
APSSPSPSAPSSPSPASPSS (SEQ ID NO: 97)

PASylation Sequence 4
SAPSSPSPSAPSSPSPASPS (SEQ ID NO: 98)

PASylation Sequence 5
SSPSAPSPSSPASPSPSSPA (SEQ ID NO: 99)

PASylation Sequence 6
AASPAAPSAPPAAASPAAPSAPPA (SEQ ID NO: 100)

PASylation Sequence 7
ASAAAPAAASAAASAPSAAA(SEQ ID NO: 101)

d) Fusion proteins

Exenatide-**FactorXa-cleavage site**-FGF21

HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPPSI **EGR**HPIPDSS PLLQFGGQVR QRYLYTDDAQ QTEAHLEIRE DGTVGGAADQ SPESLLQLKA LKPGVIQILG VKTSRFLCQR PDGALYGSLH FDPEACSFRE LLLEDGYNVY QSEAHGLPLH LPGNKSPHRD PAPRGPARFL PLPGLPPAPP EPPGILAPQP PDVGSSDPLS MVGPSQGRSP SYAS

(SEQ ID NO: 15)

His-**SUMO**-*Exenatide*- **FactorXa-cleavage site**-FGF21

MGHHHHHHGS LQ**DSEVNQEA KPEVKPEVKP ETHINLKVSD GSSEIFFKIK KTTPLRRLME AFAKRQGKEM DSLRFLYDGI RIQADQAPED LDMEDNDIIE AHREQIGG***HG EGTFTSDLSK QMEEEAVRLF IEWLKNGGPS SGAPPPS***IEG R**HPIPDSSPL LQFGGQVRQR YLYTDDAQQT EAHLEIREDG TVGGAADQSP ESLLQLKALK PGVIQILGVK TSRFLCQRPD GALYGSLHFD PEACSFRELL LEDGYNVYQS EAHGLPLHLP GNKSPHRDPA PRGPARFLPL PGLPPAPPEP PGILAPQPPD VGSSDPLSMV GPSQGRSPSY AS

(SEQ ID NO: 16)

Exenatide-FGF21

HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPPSH PIPDSSPLLQ FGGQVRQRYL YTDDAQQTEA HLEIREDGTV GGAADQSPES LLQLKALKPG VIQILGVKTS RFLCQRPDGA LYGSLHFDPE ACSFRELLLE DGYNVYQSEA HGLPLHLPGN KSPHRDPAPR GPARFLPLPG LPPAPPEPPG ILAPQPPDVG SSDPLSMVGP SQGRSPSYAS

(SEQ ID NO: 17)

His-**SUMO**-*Exenatide*-FGF21

MGHHHHHHGS LQ**DSEVNQEA KPEVKPEVKP ETHINLKVSD GSSEIFFKIK KTTPLRRLME AFAKRQGKEM DSLRFLYDGI RIQADQAPED LDMEDNDIIE AHREQIGG***HG EGTFTSDLSK QMEEEAVRLF IEWLKNGGPS SGAPPPS*HPI PDSSPLLQFG GQVRQRYLYT DDAQQTEAHL EIREDGTVGG AADQSPESLL QLKALKPGVI QILGVKTSRF LCQRPDGALY GSLHFDPEAC SFRELLLEDG YNVYQSEAHG LPLHLPGNKS PHRDPAPRGP ARFLPLPGLP PAPPEPPGIL APQPPDVGSS DPLSMVGPSQ GRSPSYAS

(SEQ ID NO: 18)

His-**SUMO**-*Exenatide*-**GGGRR**-FGF21

MGHHHHHHGS LQ**DSEVNQEA KPEVKPEVKP ETHINLKVSD GSSEIFFKIK KTTPLRRLME AFAKRQGKEM DSLRFLYDGI RIQADQAPED LDMEDNDIIE AHREQIGG***HG EGTFTSDLSK QMEEEAVRLF IEWLKNGGPS SGAPPPS***GGG RR**HPIPDSSP LLQFGGQVRQ RYLYTDDAQQ TEAHLEIRED GTVGGAADQS PESLLQLKAL KPGVIQILGV KTSRFLCQRP DGALYGSLHF DPEACSFREL LLEDGYNVYQ SEAHGLPLHL PGNKSPHRDP APRGPARFLP LPGLPPAPPE PPGILAPQPP DVGSSDPLSM VGPSQGRSPS YAS

(SEQ ID NO: 19)

Exenatide-**GGGRR**-FGF21

*HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPPS***G GGRR**HPIPDS SPLLQFGGQV
RQRYLYTDDA QQTEAHLEIR EDGTVGGAAD QSPESLLQLK ALKPGVIQIL GVKTSRFLCQ
RPDGALYGSL HFDPEACSFR ELLLEDGYNV YQSEAHGLPL HLPGNKSPHR DPAPRGPARF
LPLPGLPPAP PEPPGILAPQ PPDVGSSDPL SMVGPSQGRS PSYAS

(SEQ ID NO: 20)

His-**SUMO**-Lixisenatide-FGF21

MGHHHHHHGS LQ**DSEVNQEA KPEVKPEVKP ETHINLKVSD GSSEIFFKIK KTTPLRRLME
AFAKRQGKEM DSLRFLYDGI RIQADQAPED LDMEDNDIIE AHREQIGG***HG EGTFTSDLSK
QMEEEAVRLF IEWLKNGGPS SGAPPSKKKK KK*HPIPDSSP LLQFGGQVRQ RYLYTDDAQQ
TEAHLEIRED GTVGGAADQS PESLLQLKAL KPGVIQILGV KTSRFLCQRP DGALYGSLHF
DPEACSFREL LLEDGYNVYQ SEAHGLPLHL PGNKSPHRDP APRGPARFLP LPGLPPAPPE
PPGILAPQPP DVGSSDPLSM VGPSQGRSPS YAS

(SEQ ID NO: 21)

Lixisenatide-FGF21

*HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPSKK KKKK*HPIPDS SPLLQFGGQV
RQRYLYTDDA QQTEAHLEIR EDGTVGGAAD QSPESLLQLK ALKPGVIQIL GVKTSRFLCQ
RPDGALYGSL HFDPEACSFR ELLLEDGYNV YQSEAHGLPL HLPGNKSPHR DPAPRGPARF
LPLPGLPPAP PEPPGILAPQ PPDVGSSDPL SMVGPSQGRS PSYAS

(SEQ ID NO: 22)

His-**SUMO**- Lixisenatide- **FactorXa- cleavage site** -FGF21

MGHHHHHHGS LQ**DSEVNQEA KPEVKPEVKP ETHINLKVSD GSSEIFFKIK KTTPLRRLME
AFAKRQGKEM DSLRFLYDGI RIQADQAPED LDMEDNDIIE AHREQIGG***HG EGTFTSDLSK
QMEEEAVRLF IEWLKNGGPS SGAPPSKKKK KK***IEGR**HPIP DSSPLLQFGG QVRQRYLYTD
DAQQTEAHLE IREDGTVGGA ADQSPESLLQ LKALKPGVIQ ILGVKTSRFL CQRPDGALYG
SLHFDPEACS FRELLLEDGY NVYQSEAHGL PLHLPGNKSP HRDPAPRGPA RFLPLPGLPP
APPEPPGILA PQPPDVGSSD PLSMVGPSQG RSPSYAS

(SEQ ID NO: 23)

Lixisenatide- **FactorXa- cleavage site** -FGF21

*HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPSKK KKKK***IEGR**HP IPDSSPLLQF
GGQVRQRYLY TDDAQQTEAH LEIREDGTVG GAADQSPESL LQLKALKPGV IQILGVKTSR
FLCQRPDGAL YGSLHFDPEA CSFRELLLED GYNVYQSEAH GLPLHLPGNK SPHRDPAPRG
PARFLPLPGL PPAPPEPPGI LAPQPPDVGS SDPLSMVGPS QGRSPSYAS

(SEQ ID NO: 24)

His-**SUMO**- Lixisenatide-**GGGRR**-FGF21

MGHHHHHHGS LQ**DSEVNQEA KPEVKPEVKP ETHINLKVSD GSSEIFFKIK KTTPLRRLME
AFAKRQGKEM DSLRFLYDGI RIQADQAPED LDMEDNDIIE AHREQIGG***HG EGTFTSDLSK
QMEEEAVRLF IEWLKNGGPS SGAPPSKKKK KK**GGGRR**HPI PDSSPLLQFG GQVRQRYLYT
DDAQQTEAHL EIREDGTVGG AADQSPESLL QLKALKPGVI QILGVKTSRF LCQRPDGALY
GSLHFDPEAC SFRELLLEDG YNVYQSEAHG LPLHLPGNKS PHRDPAPRGP ARFLPLPGLP
PAPPEPPGIL APQPPDVGSS DPLSMVGPSQ GRSPSYAS

(SEQ ID NO: 25)

Lixisenatide-GGGRR-FGF21

*HGEGTFTSDL SKQMEEEAVR LFIEWLKNGG PSSGAPPSKK KKKK*GGGRRH PIPDSSPLLQ
FGGQVRQRYL YTDDAQQTEA HLEIREDGTV GGAADQSPES LLQLKALKPG VIQILGVKTS
RFLCQRPDGA LYGSLHFDPE ACSFRELLLE DGYNVYQSEA HGLPLHLPGN KSPHRDPAPR
GPARFLPLPG LPPAPPEPPG ILAPQPPDVG SSDPLSMVGP SQGRSPSYAS

(SEQ ID NO: 26)

CR9443 His-**SUMO**-FGF21-GSGSIEGR- *Exenatide* 36698,08 Da
Linker plus intact Factor Xa cleavage site
MGHHHHHHGSLQ**DSEVNQEAKPEVKPEVKPETHINLKVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRF**
LYDGIRIQADQAPEDLDMEDNDIIEAHREQIGGHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVG
GAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLH
LPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYASGSGSIEGR*HGE*
GTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS

(SEQ ID NO: 39)

CR9444 His-**SUMO**-FGF21-GSGSIEGQ- *Exenatide* 36670,02 Da
Linker plus mutated/defect Factor Xa cleavage site
MGHHHHHHGSLQ**DSEVNQEAKPEVKPEVKPETHINLKVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRF**
LYDGIRIQADQAPEDLDMEDNDIIEAHREQIGGHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVG
GAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLH
LPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYASGSGSIEGQ*HGE*
GTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS

(SEQ ID NO: 40)

CR9445 His-**SUMO** -*Exenatide*-IEGQ- FGF21 36381,76 Da
Mutated/defect Factor Xa cleavage site as linker
MMGHHHHHHGSLQ**DSEVNQEAKPEVKPEVKPETHINLKVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLR**
FLYDGIRIQADQAPEDLDMEDNDIIEAHREQIGG*HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS*IE
GQHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRF
LCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPE
PPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 41)

CR9446 His-**SUMO**- *Exenatide* -APASPAS-FGF21 36535,93 Da
Linker based on PAS sequence
MMGHHHHHHGSLQ**DSEVNQEAKPEVKPEVKPETHINLKVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLR**
FLYDGIRIQADQAPEDLDMEDNDIIEAHREQIGG*HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS*AP
ASPASHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKT
SRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPA
PPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 42)

CR9447 His-**SUMO**- *Exenatide* -APASCPAS- FGF21 36638,07 Da
Linker based on PAS sequence plus Cystein for potential modification
MGHHHHHHGSLQ**DSEVNQEAKPEVKPEVKPETHINLKVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRF**
LYDGIRIQADQAPEDLDMEDNDIIEAHREQIGG*HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS*APA
SCPASHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKT
SRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPA
PPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 43)

CR9448 His-**SUMO** -*Exenatide*-GSGS- FGF21 36242,57 Da
GSGS-linker
MGHHHHHHGSLQ**DSEVNQEAKPEVKPEVKPETHINLKVSDGSSEIFFKIKKTTPLRRLMEAFAKRQGKEMDSLRF**
LYDGIRIQADQAPEDLDMEDNDIIEAHREQIGG*HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS*GSG
SHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFL
CQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEP
PGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 44)

FGF21-GSGSIEGR-Exenatide 24306,16 Da
(GSGSIEGR = linker)
HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGV
KTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARF
LPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYASGSGSIEGRHGEGTFTSDLSKQME
EEAVRLFIEWLKNGGPSSGAPPPS

(SEQ ID NO: 45)

FGF21-GSGSIEGQ-Exenatide 24278,10 Da
(GSGSIEGQ = linker)
HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGV
KTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARF
LPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYASGSGSIEGQHGEGTFTSDLSKQME
EEAVRLFIEWLKNGGPSSGAPPPS

(SEQ ID NO: 46)

Exenatide-IEGQ-FGF21 23989,84 Da
(IEGQ = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSIEGQHPIPDSSPLLQFGGQVRQRYLYTDD
AQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEAC
SFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVG
SSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 47)

Exenatide-APASPAS-FGF21 24144,01 Da
(APASPAS = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSAPASPASHPIPDSSPLLQFGGQVRQRYLY
TDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDP
EACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPP
DVGSSDPLSMVGPSQGRSPSYAS (SEQ ID NO: 48)

Exenatide-APASCPAS-FGF21 24246,14 Da
(APASCPAS = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSAPASCPASHPIPDSSPLLQFGGQVRQRYL
YTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFD
PEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQP
PDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 49)

Exenatide-GSGS-FGF21 23850,64 Da
(GSGS = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGSGSHPIPDSSPLLQFGGQVRQRYLYTDD
AQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEAC
SFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVG
SSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 50)

Exenatide-GG-ABD-GG-FGF21 28820,40 Da
(GG-ABD-GG = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGLAEAKVLANRELDKYGVSDYYKNLINN
AKTVEGVKALIDEILAALPGGHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQ
SPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLP
LHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 51)

Exenatide-GGGGS-ABD-GGGGS-FGF21 29222,76 Da
(GGGGS-ABD-GGGGS = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGSLAEAKVLANRELDKYGVSDYYKNL
INNAKTVEGVKALIDEILAALPGGGGSHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTV
GGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQS
EAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSP
SYAS

(SEQ ID NO: 52)

Exenatide-FGF21-GG-ABD 28706,29 Da
(GG-ABD = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSHPIPDSSPLLQFGGQVRQRYLYTDDAQQT
EAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRE
LLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDP
LSMVGPSQGRSPSYASGGLAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALP

(SEQ ID NO: 53)

Exenatide-FGF21-GGGGS-ABD 28907,48 Da
(GGGGS-ABD = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSHPIPDSSPLLQFGGQVRQRYLYTDDAQQT
EAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRE
LLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDP
LSMVGPSQGRSPSYASGGGGSLAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALP

(SEQ ID NO: 54)

Exenatide-FGF21-GG-ABD-GG-FGF21 48195,17 Da
(GG-ABD-GG = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSHPIPDSSPLLQFGGQVRQRYLYTDDAQQT
EAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRE
LLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDP
LSMVGPSQGRSPSYASGGLAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALPGGHP
IPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKT
SRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLP
LPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 55)

Exenatide-FGF21-GGGGS-ABD-GGGGS-FGF21 48597,54 Da
(GGGGS-ABD-GGGGS = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSHPIPDSSPLLQFGGQVRQRYLYTDDAQQT
EAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRE
LLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDP
LSMVGPSQGRSPSYASGGGGSLAEAKVLANRELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALPG
GGGSHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQ
ILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRG
PARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 56)

Exenatide- GGGGS-His-GGGGS -FGF21 25134,92 Da
(GGGGS-His-GGGGS = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGSHAHGHGHAHGGGGSHPIPDSSPLL
QFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRP
DGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAP
PEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 57)

Exenatide-GGGGS-His-GGGGS-ABD-GG-FGF21 30278,83 Da
(GGGGS-His-GGGGS-ABD-GG = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGGGSHAHGHGHAHGGGGSLAEAKVLANR
ELDKYGVSDYYKNLINNAKTVEGVKALIDEILAALPGGHPIPDSSPLLQFGGQVRQRYLYTDDAQQTE
AHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFREL
LLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPL
SMVGPSQGRSPSYAS (SEQ ID NO: 58)

Exenatide-$(B)_{0-1000}$-FGF21 mutein-Cys
(B = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS(B)HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHL
EIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQ
SEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYA**C**

(SEQ ID NO: 59)

Exenatide-$(B)_{0-1000}$-FGF21 mutein-Lys
(B = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPS(B)HPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHL
EIREDGTVGGAADQSPESLLQLRALRPGVIQILGVRTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQ
SEAHGLPLHLPGNRSPHRDPKPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 60)

Exenatide-GG-Cys-$(G)_{21}$-FGF21 25009,73 Da
(GG-Cys-$(G)_{21}$ = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGG**C**GGGGGGGGGSGGGGSGGGGSHPIPDSSPLLQFG
GQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHF
DPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSS
DPLSMVGPSQGRSPSYAS

(SEQ ID NO: 61)

Exenatide-GG-Lys-$(G)_{21}$-FGF21 25035,78 Da
(GG-Lys-$(G)_{21}$ = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGKGGGGGGGGGSGGGGSGGGGSHPIPDS
SPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFL
CQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGL
PPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

(SEQ ID NO: 62)

Exenatide-IgG 1 Asp103-Lys329-FGF21 49314,49 Da
(GG-IgG 1 Asp103-Lys329-GG = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGDKTHTCPPCPAPELLGGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN
GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES
NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGHP
IPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKT
SRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLP
LPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS (SEQ ID NO: 63)

Exenatide-IgG1 Pro120-Lys329-FGF21 47598,53 Da
(GG-IgG1 Pro120-Lys329-GG = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDS
DGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGHPIPDSSPLLQFGGQVRQR
YLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLH
FDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAP
QPPDVGSSDPLSMVGPSQGRSPSYAS (SEQ ID NO: 64)

Exenatide-IgG1 Pro120-Lys329 mutated-FGF21 47572,41 Da
(GG-IgG1 Pro120-Lys329 mutated-GG = linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTSPPSRDELTKNQVSLRCHVKGFYPSDIAVEWESNGQPENNYKTTKPVLDS
DGSFELKSALTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGKGGHPIPDSSPLLQFGGQVRQR
YLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLH
FDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHRDPAPRGPARFLPLPGLPPAPPEPPGILAP
QPPDVGSSDPLSMVGPSQGRSPSYAS (SEQ ID NO: 65)

Exenatide- IgG1 Pro120-Lys222-FGF21 35541,10 Da
(GG-IgG1 Pro120-Lys222-GG linker)
HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPPSGGPSVFLFPPKPKDTLMISRTPEVTCVVV
DVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGGHPIPDSSPLLQFGGQVRQRYLYTDDAQQTEAHLEIREDGTVGGAADQSPESLLQLKAL
KPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEACSFRELLLEDGYNVYQSEAHGLPLHLPGNKSPHR
DPAPRGPARFLPLPGLPPAPPEPPGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS
(SEQ ID NO: 66)

e) Constructs for fusion proteins (DNA sequences)

Construct: CR8829

ATGGGC*CATCACCATCACCATCAC*GGAAGCCTGCAGGATAGCGAAGTTAATCAGGAAGCAAAACCGGAAGTTAAA
CCGGAAGTTAAACCGGAAACCCATATTAATCTGAAAGTTAGCGATGGTAGCAGCGAAATTTTTTTTAAAATTAAA
AAAACCACCCCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCACATCGTGAACAGATTGGTGGTCATGGTGAAGGTACATTCACATCTGATCTATCAAAACAAATGGAAGAAGAA
GCTGTTAGACTATTCATTGAATGGTTGAAAAATGGTGGTCCATCTTCAGGTGCTCCACCTCCAAGTATCGAAGGT
CGTCAC*CCCATCCCTGACTCCAGTCCTCTCCTGCAATTCGGGGGCCAAGTCCGGCAGCGGTACCTCTACACAGAT*
GATGCCCAGCAGACAGAAGCCCACCTGGAGATCAGGGAGGATGGGACGGTGGGGGGCGCTGCTGACCAGAGCCCC
GAAAGTCTCCTGCAGCTGAAAGCCTTGAAGCCGGGAGTTATTCAAATCTTGGGAGTCAAGACATCCAGGTTCCTG
TGCCAGCGGCCAGATGGGGCCCTGTATGGATCGCTCCACTTTGACCCTGAGGCCTGCAGCTTCCGGGAGCTGCTT
CTTGAGGACGGATACAATGTTTACCAGTCCGAAGCCCACGGCCTCCCGCTGCACCTGCCAGGGAACAAGTCCCCA
CACCGGGACCCTGCACCCCGAGGACCAGCTCGCTTCCTGCCACTACCAGGCCTGCCCCCCGCACCCCCGGAGCCA
CCCGGAATCCTGGCCCCCCAGCCCCCCGATGTGGGCTCCTCGGACCCTCTGAGCATGGTGGGACCTTCCCAGGGC
*CGAAGCCCCAGCTACGCTTCC*TGA

(SEQ ID NO: 27)

Construct: CR8846

ATGGGC*CATCACCATCACCATCAC*GGAAGCCTGCAGGATAGCGAAGTTAATCAGGAAGCAAAACCGGAAGTTAAA
CCGGAAGTTAAACCGGAAACCCATATTAATCTGAAAGTTAGCGATGGTAGCAGCGAAATTTTTTTTAAAATTAAA
AAAACCACCCCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCACATCGTGAACAGATTGGTGGTCATGGTGAAGGTACATTCACATCTGATCTATCAAAACAAATGGAAGAAGAA
GCTGTTAGACTATTCATTGAATGGTTGAAAAATGGTGGTCCATCTTCAGGTGCTCCACCTCCAAGTCACCCCATC
CCTGACTCCAGTCCTCTCCTGCAATTCGGGGGCCAAGTCCGGCAGCGGTACCTCTACACAGATGATGCCCAGCAG
ACAGAAGCCCACCTGGAGATCAGGGAGGATGGGACGGTGGGGGGCGCTGCTGACCAGAGCCCCGAAAGTCTCCTG
CAGCTGAAAGCCTTGAAGCCGGGAGTTATTCAAATCTTGGGAGTCAAGACATCCAGGTTCCTGTGCCAGCGGCCA
GATGGGGCCCTGTATGGATCGCTCCACTTTGACCCTGAGGCCTGCAGCTTCCGGGAGCTGCTTCTTGAGGACGGA
TACAATGTTTACCAGTCCGAAGCCCACGGCCTCCCGCTGCACCTGCCAGGGAACAAGTCCCCACACCGGGACCCT
GCACCCCGAGGACCAGCTCGCTTCCTGCCACTACCAGGCCTGCCCCCCGCACCCCCGGAGCCACCCGGAATCCTG
GCCCCCCAGCCCCCCGATGTGGGCTCCTCGGACCCTCTGAGCATGGTGGGACCTTCCCAGGGCCGAAGCCCCAGC
TACGCTTCCTGA

(SEQ ID NO: 28)

Construct: CR8847

ATGGGCCATCACCATCACCATCACGGAAGCCTGCAGGATAGCGAAGTTAATCAGGAAGCAAAACCGGAAGTTAAA
CCGGAAGTTAAACCGGAAACCCATATTAATCTGAAAGTTAGCGATGGTAGCAGCGAAATTTTTTTTAAAATTAAA
AAAACCACCCCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCACATCGTGAACAGATTGGTGGTCATGGTGAAGGTACATTCACATCTGATCTATCAAAACAAATGGAAGAAGAA
GCTGTTAGACTATTCATTGAATGGTTGAAAAATGGTGGTCCATCTTCAGGTGCTCCACCTCCAAGTGGGGGCGGG
CGCCGACACCCCATCCCTGACTCCAGTCCTCTCCTGCAATTCGGGGGCCAAGTCCGGCAGCGGTACCTCTACACA
GATGATGCCCAGCAGACAGAAGCCCACCTGGAGATCAGGGAGGATGGGACGGTGGGGGGCGCTGCTGACCAGAGC
CCCGAAAGTCTCCTGCAGCTGAAAGCCTTGAAGCCGGGAGTTATTCAAATCTTGGGAGTCAAGACATCCAGGTTC
CTGTGCCAGCGGCCAGATGGGGCCCTGTATGGATCGCTCCACTTTGACCCTGAGGCCTGCAGCTTCCGGGAGCTG
CTTCTTGAGGACGGATACAATGTTTACCAGTCCGAAGCCCACGGCCTCCCGCTGCACCTGCCAGGGAACAAGTCC
CCACACCGGGACCCTGCACCCCGAGGACCAGCTCGCTTCCTGCCACTACCAGGCCTGCCCCCCGCACCCCCGGAG
CCACCCGGAATCCTGGCCCCCCAGCCCCCCGATGTGGGCTCCTCGGACCCTCTGAGCATGGTGGGACCTTCCCAG
GGCCGAAGCCCCAGCTACGCTTCCTGA

(SEQ ID NO: 29)

Construct: CR8848

ATGGGCCATCACCATCACCATCACGGAAGCCTGCAGGATAGCGAAGTTAATCAGGAAGCAAAACCGGAAGTTAAA
CCGGAAGTTAAACCGGAAACCCATATTAATCTGAAAGTTAGCGATGGTAGCAGCGAAATTTTTTTTAAAATTAAA
AAAACCACCCCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCACATCGTGAACAGATTGGTGGTCACGGTGAAGGTACCTTCACCTCCGACCTGTCCAAACAGATGGAAGAAGAA
GCTGTTCGTCTGTTCATCGAATGGCTGAAAAACGGTGGTCCGTCCTCCGGTGCTCCGCCTTCGAAAAAGAAGAAA
AAGAAACACCCCATCCCTGACTCCAGTCCTCTCCTGCAATTCGGGGGCCAAGTCCGGCAGCGGTACCTCTACACA
GATGATGCCCAGCAGACAGAAGCCCACCTGGAGATCAGGGAGGATGGGACGGTGGGGGGCGCTGCTGACCAGAGC
CCCGAAAGTCTCCTGCAGCTGAAAGCCTTGAAGCCGGGAGTTATTCAAATCTTGGGAGTCAAGACATCCAGGTTC
CTGTGCCAGCGGCCAGATGGGGCCCTGTATGGATCGCTCCACTTTGACCCTGAGGCCTGCAGCTTCCGGGAGCTG
CTTCTTGAGGACGGATACAATGTTTACCAGTCCGAAGCCCACGGCCTCCCGCTGCACCTGCCAGGGAACAAGTCC
CCACACCGGGACCCTGCACCCCGAGGACCAGCTCGCTTCCTGCCACTACCAGGCCTGCCCCCCGCACCCCCGGAG
CCACCCGGAATCCTGGCCCCCCAGCCCCCCGATGTGGGCTCCTCGGACCCTCTGAGCATGGTGGGACCTTCCCAG
GGCCGAAGCCCCAGCTACGCTTCCTGA

(SEQ ID NO: 30)

Construct: CR8849

ATGGGCCATCACCATCACCATCACGGAAGCCTGCAGGATAGCGAAGTTAATCAGGAAGCAAAACCGGAAGTTAAA
CCGGAAGTTAAACCGGAAACCCATATTAATCTGAAAGTTAGCGATGGTAGCAGCGAAATTTTTTTTAAAATTAAA
AAAACCACCCCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCACATCGTGAACAGATTGGTGGTCACGGTGAAGGTACCTTCACCTCCGACCTGTCCAAACAGATGGAAGAAGAA
GCTGTTCGTCTGTTCATCGAATGGCTGAAAAACGGTGGTCCGTCCTCCGGTGCTCCGCCTTCGAAAAAGAAGAAA
AAGAAAATCGAAGGTCGTCACCCCATCCCTGACTCCAGTCCTCTCCTGCAATTCGGGGGCCAAGTCCGGCAGCGG
TACCTCTACACAGATGATGCCCAGCAGACAGAAGCCCACCTGGAGATCAGGGAGGATGGGACGGTGGGGGGCGCT
GCTGACCAGAGCCCCGAAAGTCTCCTGCAGCTGAAAGCCTTGAAGCCGGGAGTTATTCAAATCTTGGGAGTCAAG
ACATCCAGGTTCCTGTGCCAGCGGCCAGATGGGGCCCTGTATGGATCGCTCCACTTTGACCCTGAGGCCTGCAGC
TTCCGGGAGCTGCTTCTTGAGGACGGATACAATGTTTACCAGTCCGAAGCCCACGGCCTCCCGCTGCACCTGCCA
GGGAACAAGTCCCCACACCGGGACCCTGCACCCCGAGGACCAGCTCGCTTCCTGCCACTACCAGGCCTGCCCCCC
GCACCCCCGGAGCCACCCGGAATCCTGGCCCCCCAGCCCCCCGATGTGGGCTCCTCGGACCCTCTGAGCATGGTG
GGACCTTCCCAGGGCCGAAGCCCCAGCTACGCTTCCTGA

(SEQ ID NO: 31)

Construct: CR8850

ATGGGCCATCACCATCACCATCACGGAAGCCTGCAGGATAGCGAAGTTAATCAGGAAGCAAAACCGGAAGTTAAA
CCGGAAGTTAAACCGGAAACCCATATTAATCTGAAAGTTAGCGATGGTAGCAGCGAAATTTTTTTTAAAATTAAA
AAAACCACCCCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCACATCGTGAACAGATTGGTGGTCACGGTGAAGGTACCTTCACCTCCGACCTGTCCAAACAGATGGAAGAAGAA
GCTGTTCGTCTGTTCATCGAATGGCTGAAAAACGGTGGTCCGTCCTCCGGTGCTCCGCCTTCGAAAAAGAAGAAA
AAGAAAGGGGGCGGGAGAAGGCACCCCATCCCTGACTCCAGTCCTCTCCTGCAATTCGGGGGCCAAGTCCGGCAG
CGGTACCTCTACACAGATGATGCCCAGCAGACAGAAGCCCACCTGGAGATCAGGGAGGATGGGACGGTGGGGGGC
GCTGCTGACCAGAGCCCCGAAAGTCTCCTGCAGCTGAAAGCCTTGAAGCCGGGAGTTATTCAAATCTTGGGAGTC
AAGACATCCAGGTTCCTGTGCCAGCGGCCAGATGGGGCCCTGTATGGATCGCTCCACTTTGACCCTGAGGCCTGC
AGCTTCCGGGAGCTGCTTCTTGAGGACGGATACAATGTTTACCAGTCCGAAGCCCACGGCCTCCCGCTGCACCTG
CCAGGGAACAAGTCCCCACACCGGGACCCTGCACCCCGAGGACCAGCTCGCTTCCTGCCACTACCAGGCCTGCCC
CCCGCACCCCCGGAGCCACCCGGAATCCTGGCCCCCCAGCCCCCCGATGTGGGCTCCTCGGACCCTCTGAGCATG
GTGGGACCTTCCCAGGGCCGAAGCCCCAGCTACGCTTCCTGA

(SEQ ID NO: 32)

Construct: CR9443

ATGGGACACCACCATCATCATCATGGTAGCCTGCAGGATAGCGAAGTTAATCAAGAAGCAAAACCGGAAGTTAAA
CCGGAAGTGAAACCGGAAACCCATATTAATCTGAAAGTTAGTGATGGCAGCAGCGAAATTTTCTTTAAAATCAAA
AAAACCACACCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCCCATCGTGAACAAATTGGTGGTCATCCGATTCCGGATAGCAGTCCGCTGCTGCAGTTTGGTGGTCAGGTTCGT
CAGCGTTATCTGTATACCGATGATGCACAGCAGACCGAAGCACATCTGGAAATTCGTGAAGATGGCACCGTTGGT
GGTGCAGCAGATCAGAGTCCGGAAAGCCTGCTGCAGCTGAAAGCACTGAAACCGGGTGTTATTCAGATTCTGGGT
GTTAAAACCAGCCGTTTTCTGTGTCAGCGTCCGGATGGTGCACTGTATGGTAGTCTGCATTTTGATCCGGAAGCA
TGTAGCTTTCGTGAACTGCTGCTGGAAGATGGTTATAATGTTTATCAGAGTGAAGCACATGGTCTGCCGCTGCAT
CTGCCTGGTAATAAAAGTCCGCATCGTGATCCGGCACCGCGTGGTCCGGCACGTTTTCTGCCTCTGCCTGGTCTG
CCTCCGGCACCTCCGGAACCTCCGGGTATTCTGGCACCGCAGCCTCCGGATGTTGGTAGCAGCGATCCGCTGAGC
ATGGTGGGTCCTAGCCAGGGTCGTAGCCCGAGCTATGCAAGCGGTAGCGGTAGCATTGAAGGTCGTCATGGTGAA
GGCACCTTTACCAGCGATCTGAGCAAACAAATGGAAGAAGAAGCAGTTCGTCTGTTTATTGAATGGCTGAAAAAT
GGTGGTCCGAGCAGTGGTGCACCTCCTCCGAGCTAA

(SEQ ID NO: 33)

Construct: CR9444

TGGGACACCACCATCATCATCATGGTAGCCTGCAGGATAGCGAAGTTAATCAAGAAGCAAAACCGGAAGTTAAAC
CGGAAGTGAAACCGGAAACCCATATTAATCTGAAAGTTAGTGATGGCAGCAGCGAAATTTTCTTTAAAATCAAAA
AAACCACACCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTTC
TGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAAG
CCCATCGTGAACAAATTGGTGGTCATCCGATTCCGGATAGCAGTCCGCTGCTGCAGTTTGGTGGTCAGGTTCGTC
AGCGTTATCTGTATACCGATGATGCACAGCAGACCGAAGCACATCTGGAAATTCGTGAAGATGGCACCGTTGGTG
GTGCAGCAGATCAGAGTCCGGAAAGCCTGCTGCAGCTGAAAGCACTGAAACCGGGTGTTATTCAGATTCTGGGTG
TTAAAACCAGCCGTTTTCTGTGTCAGCGTCCGGATGGTGCACTGTATGGTAGTCTGCATTTTGATCCGGAAGCAT
GTAGCTTTCGTGAACTGCTGCTGGAAGATGGTTATAATGTTTATCAGAGTGAAGCACATGGTCTGCCGCTGCATC
TGCCTGGTAATAAAAGTCCGCATCGTGATCCGGCACCGCGTGGTCCGGCACGTTTTCTGCCTCTGCCTGGTCTGC
CTCCGGCACCTCCGGAACCTCCGGGTATTCTGGCACCGCAGCCTCCGGATGTTGGTAGCAGCGATCCGCTGAGCA
TGGTGGGTCCTAGCCAGGGTCGTAGCCCGAGCTATGCAAGCGGTAGCGGTAGCATTGAAGGTCAGCATGGTGAAG
GCACCTTTACCAGCGATCTGAGCAAACAAATGGAAGAAGAAGCAGTTCGTCTGTTTATTGAATGGCTGAAAAATG
GTGGTCCGAGCAGTGGTGCACCTCCTCCGAGCTAA

(SEQ ID NO: 34)

Construct: CR9445

ATGGGACACCACCATCATCATCATGGTAGCCTGCAGGATAGCGAAGTTAATCAAGAAGCAAAACCGGAAGTTAAA
CCGGAAGTGAAACCGGAAACCCATATTAATCTGAAAGTTAGTGATGGCAGCAGCGAAATTTTCTTTAAAATCAAA
AAAACCACACCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCCCATCGTGAACAAATTGGTGGTCATGGTGAAGGCACCTTTACCAGCGATCTGAGCAAACAAATGGAAGAAGAA
GCAGTTCGTCTGTTTATTGAATGGCTGAAAAATGGTGGTCCGAGCAGTGGTGCACCTCCTCCGAGCATTGAAGGT
CAGCATCCGATTCCGGATAGCAGTCCGCTGCTGCAGTTTGGTGGTCAGGTTCGTCAGCGTTATCTGTATACCGAT
GATGCACAGCAGACCGAAGCACATCTGGAAATTCGTGAAGATGGCACCGTTGGTGGTGCAGCAGATCAGAGTCCG
GAAAGCCTGCTGCAGCTGAAAGCACTGAAACCGGGTGTTATTCAGATTCTGGGTGTTAAAACCAGCCGTTTTCTG
TGTCAGCGTCCGGATGGTGCACTGTATGGTAGTCTGCATTTTGATCCGGAAGCATGTAGCTTTCGTGAACTGCTG
CTGGAAGATGGTTATAATGTTTATCAGAGCGAAGCACATGGTCTGCCTCTGCATCTGCCTGGTAATAAAAGTCCG
CATCGTGATCCGGCACCGCGTGGTCCGGCACGTTTTCTGCCGCTGCCTGGTCTGCCTCCGGCACCTCCGGAACCT
CCGGGTATTCTGGCACCGCAGCCTCCGGATGTTGGTAGCAGCGATCCGCTGAGCATGGTTGGTCCGAGCCAGGGT
CGTAGCCCGAGCTATGCAAGCTAA

(SEQ ID NO: 35)

Construct: CR9446

ATGGGACACCACCATCATCATCATGGTAGCCTGCAGGATAGCGAAGTTAATCAAGAAGCAAAACCGGAAGTTAAA
CCGGAAGTGAAACCGGAAACCCATATTAATCTGAAAGTTAGTGATGGCAGCAGCGAAATTTTCTTTAAAATCAAA
AAAACCACACCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCCCATCGTGAACAAATTGGTGGTCATGGTGAAGGCACCTTTACCAGCGATCTGAGCAAACAAATGGAAGAAGAA
GCAGTTCGTCTGTTTATTGAATGGCTGAAAAATGGTGGTCCGAGCAGTGGTGCACCTCCTCCGAGCGCACCTGCC
AGCCCTGCAAGCCATCCGATTCCGGATAGCAGTCCGCTGCTGCAGTTTGGTGGTCAGGTTCGTCAGCGTTATCTG
TATACCGATGATGCACAGCAGACCGAAGCACATCTGGAAATTCGTGAAGATGGCACCGTTGGTGGTGCAGCAGAT
CAGAGTCCGGAAAGCCTGCTGCAGCTGAAAGCACTGAAACCGGGTGTTATTCAGATTCTGGGTGTTAAAACCAGC
CGTTTTCTGTGTCAGCGTCCGGATGGTGCACTGTATGGTAGTCTGCATTTTGATCCGGAAGCATGTAGCTTTCGT
GAACTGCTGCTGGAAGATGGTTATAATGTTTATCAGAGCGAAGCACATGGTCTGCCTCTGCATCTGCCTGGTAAT
AAAAGTCCGCATCGTGATCCGGCACCGCGTGGTCCGGCACGTTTTCTGCCGCTGCCTGGTCTGCCTCCGGCACCT
CCGGAACCTCCGGGTATTCTGGCACCGCAGCCTCCGGATGTTGGTAGCAGCGATCCGCTGAGCATGGTTGGTCCG
AGCCAGGGTCGTAGCCCGAGCTATGCAAGCTAA

(SEQ ID NO: 36)

Construct: CR9447

ATGGGACACCACCATCATCATCATGGTAGCCTGCAGGATAGCGAAGTTAATCAAGAAGCAAAACCGGAAGTTAAA
CCGGAAGTGAAACCGGAAACCCATATTAATCTGAAAGTTAGTGATGGCAGCAGCGAAATTTTCTTTAAAATCAAA
AAAACCACACCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCCCATCGTGAACAAATTGGTGGTCATGGTGAAGGCACCTTTACCAGCGATCTGAGCAAACAAATGGAAGAAGAA
GCAGTTCGTCTGTTTATTGAATGGCTGAAAAATGGTGGTCCGAGCAGTGGTGCACCTCCTCCGAGCGCACCGGCA
AGCTGTCCGGCAAGCCATCCGATTCCGGATAGCAGTCCGCTGCTGCAGTTTGGTGGTCAGGTTCGTCAGCGTTAT
CTGTATACCGATGATGCACAGCAGACCGAAGCACATCTGGAAATTCGTGAAGATGGCACCGTTGGTGGTGCAGCA
GATCAGAGTCCGGAAAGCCTGCTGCAGCTGAAAGCACTGAAACCGGGTGTTATTCAGATTCTGGGTGTTAAAACC
AGCCGTTTTCTGTGTCAGCGTCCGGATGGTGCACTGTATGGTAGTCTGCATTTTGATCCGGAAGCATGTAGCTTT
CGTGAACTGCTGCTGGAAGATGGTTATAATGTTTATCAGAGCGAAGCACATGGTCTGCCTCTGCATCTGCCTGGT
AATAAAAGTCCGCATCGTGATCCGGCACCGCGTGGTCCGGCACGTTTTCTGCCGCTGCCTGGTCTGCCTCCGGCA
CCTCCGGAACCTCCGGGTATTCTGGCACCGCAGCCTCCGGATGTTGGTAGCAGCGATCCGCTGAGCATGGTTGGT
CCGAGCCAGGGTCGTAGCCCGAGCTATGCAAGCTAA

(SEQ ID NO: 37)

Construct: CR9448

ATGGGACACCACCATCATCATCATGGTAGCCTGCAGGATAGCGAAGTTAATCAAGAAGCAAAACCGGAAGTTAAA
CCGGAAGTGAAACCGGAAACCCATATTAATCTGAAAGTTAGTGATGGCAGCAGCGAAATTTTCTTTAAAATCAAA
AAAACCACACCGCTGCGTCGTCTGATGGAAGCATTTGCAAAACGTCAGGGTAAAGAAATGGATAGCCTGCGTTTT
CTGTATGATGGTATTCGTATTCAGGCAGATCAGGCACCGGAAGATCTGGATATGGAAGATAATGATATTATTGAA
GCCCATCGTGAACAAATTGGTGGTCATGGTGAAGGCACCTTTACCAGCGATCTGAGCAAACAAATGGAAGAAGAA
GCAGTTCGTCTGTTTATTGAATGGCTGAAAAATGGTGGTCCGAGCAGTGGTGCACCTCCTCCGAGCGGTAGCGGT
AGCCATCCGATTCCGGATAGCAGTCCGCTGCTGCAGTTTGGTGGTCAGGTTCGTCAGCGTTATCTGTATACCGAT
GATGCACAGCAGACCGAAGCACATCTGGAAATTCGTGAAGATGGCACCGTTGGTGGTGCAGCAGATCAGAGTCCG
GAAAGCCTGCTGCAGCTGAAAGCACTGAAACCGGGTGTTATTCAGATTCTGGGTGTTAAAACCAGCCGTTTTCTG
TGTCAGCGTCCGGATGGTGCACTGTATGGTAGTCTGCATTTTGATCCGGAAGCATGTAGCTTTCGTGAACTGCTG
CTGGAAGATGGTTATAATGTTTATCAGAGCGAAGCACATGGTCTGCCTCTGCATCTGCCTGGTAATAAAAGTCCG
CATCGTGATCCGGCACCGCGTGGTCCGGCACGTTTTCTGCCGCTGCCTGGTCTGCCTCCGGCACCTCCGGAACCT
CCGGGTATTCTGGCACCGCAGCCTCCGGATGTTGGTAGCAGCGATCCGCTGAGCATGGTTGGTCCGAGCCAGGGT
CGTAGCCCGAGCTATGCAAGCTAA

(SEQ ID NO: 38)

Exenatide-GGGGS-ABD-GGGGS-FGF21 (DNA sequence)

CACGGCGAGGGCACCTTCACCAGCGACCTGAGCAAGCAGATGGAAGAGGAAGCCGTGCGGCTGTTCATCGAGTGG
CTGAAGAATGGCGGCCCTAGCTCTGGCGCCCCTCCACCTTCTGGCGGCGGAGGATCTCTGGCCGAAGCCAAGGTG
CTGGCCAACAGAGAGCTGGATAAGTACGGCGTGTCCGACTACTACAAGAACCTGATCAACAACGCCAAGACCGTG
GAAGGCGTGAAGGCCCTGATCGACGAGATTCTGGCTGCCCTGCCTGGCGGAGGGGGCTCTCATCCTATCCCTGAT
AGCAGCCCCCTGCTGCAGTTTGGCGGACAAGTGCGGCAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAG
GCCCACCTGGAAATCAGAGAAGATGGCACCGTGGGCGGAGCCGCCGATCAGTCTCCTGAATCTCTGCTGCAGCTG
AAAGCCCTGAAGCCCGGCGTGATCCAGATCCTGGGCGTGAAAACCAGCCGGTTCCTGTGCCAGAGGCCTGACGGC
GCCCTGTATGGCAGCCTGCACTTTGATCCTGAGGCCTGCAGCTTTAGAGAGCTGCTGCTGGAGGACGGCTACAAC
GTGTACCAGTCTGAGGCCCACGGCCTGCCCCTGCATCTGCCTGGAAACAAGAGCCCCCACAGAGATCCCGCCCCT
AGAGGCCCTGCCAGATTCCTGCCTCTGCCCGGACTGCCTCCTGCCCCTCCTGAACCTCCTGGAATTCTGGCCCCC
CAGCCTCCTGATGTGGGCAGCTCTGATCCCCTGAGCATGGTGGGACCTAGCCAGGGCAGAAGCCCTAGCTACGCC
AGCTAATGAA

(SEQ ID NO: 67)

Exenatide-FGF21-GGGGS-ABD (DNA sequence)

CACGGCGAGG GCACCTTCAC CAGCGACCTG AGCAAGCAGA TGGAAGAGGA AGCCGTGCGG
CTGTTCATCG AGTGGCTGAA GAATGGCGGC CCTAGCTCTG GCGCCCCTCC TCCTTCACAC
CCCATCCCTG ATAGCAGCCC CCTGCTGCAG TTTGGCGGAC AAGTGCGGCA GAGATACCTG
TACACCGACG ACGCCCAGCA GACCGAGGCC CACCTGGAAA TCAGAGAAGA TGGCACCGTG
GGCGGAGCCG CCGATCAGTC TCCTGAATCT CTGCTGCAGC TGAAGGCCCT GAAGCCCGGC
GTGATCCAGA TCCTGGGCGT GAAAACCAGC CGGTTCCTGT GCCAGAGGCC TGACGGCGCC
CTGTATGGCA GCCTGCACTT TGATCCTGAG GCCTGCAGCT TCAGAGAGCT GCTGCTGGAG
GACGGCTACA ACGTGTACCA GTCTGAGGCC CACGGCCTGC CCCTGCATCT GCCTGGAAAC
AAGAGCCCCC ACAGAGATCC CGCCCCTAGA GGCCCTGCCA GATTCCTGCC ACTGCCTGGA
CTGCCTCCAG CCCCTCCTGA GCCTCCTGGA ATTCTGGCTC CCCAGCCTCC TGATGTGGGC
AGCAGCGATC CTCTGAGCAT GGTGGGACCT AGCCAGGGCA GAAGCCCTAG CTACGCTTCT
GGCGGCGGAG GATCTCTGGC CGAGGCTAAG GTGCTGGCCA ATAGAGAGCT GGATAAGTAC
GGCGTGTCCG ACTACTACAA GAACCTGATC AACAACGCCA AGACCGTGGA AGGCGTGAAA
GCCCTGATCG ACGAGATCCT GGCCGCCCTG CCCTAATGA

(SEQ ID NO: 68)

Exenatide-FGF21-GGGGS-ABD-GGGGS-FGF21 (DNA sequence)

CACGG CGAGGGCACCTTCACCAGCG ACCTGAGCAA GCAGATGGAA GAGGAAGCCG TGCGGCTGTT
CATCGAGTGG CTGAAGAATG GCGGCCCTAG CTCTGGCGCC CCTCCTCCTTCACACCCCAT CCCTGATAGC
AGCCCCCTGC TGCAGTTTGG CGGACAAGTG CGGCAGAGAT ACCTGTACAC CGACGACGCC
CAGCAGACCG AGGCCCACCTGGAAATCAGA GAAGATGGCA CCGTGGGCGG AGCCGCCGAT CAGTCTCCTG
AATCTCTGCT GCAGCTGAAG GCCCTGAAGC CCGGCGTGAT CCAGATCCTGGGCGTGAAAA CCAGCCGGTT
CCTGTGCCAG AGGCCTGACG GCGCCCTGTA TGGCAGCCTG CACTTTGATC CTGAGGCCTG
CAGCTTCAGA GAGCTGCTGCTGGAGGACGG CTACAACGTG TACCAGTCTG AGGCCCACGG CCTGCCCCTG
CATCTGCCTG GAAACAAGAG CCCCCACAGA GATCCCGCCC CTAGAGGCCCTGCCAGATTC CTGCCACTGC
CTGGACTGCC TCCAGCCCCT CCTGAGCCTC CTGGAATTCT GGCTCCCCAG CCTCCTGATG
TGGGCAGCAG CGATCCTCTGAGCATGGTGG GACCTAGCCA GGGCAGAAGC CCTAGCTACG CTTCTGGCGG
CGGAGGATCT CTGGCCGAGG CTAAGGTGCT GGCCAATAGA GAGCTGGATAAGTACGGCGT GTCCGACTAC
TACAAGAACC TGATCAACAA CGCCAAGACC GTGGAAGGCG TGAAAGCCCT GATCGACGAG
ATCCTGGCTG CTCTGCCAGGCGGAGGGGGA TCTCACCCTA TCCCAGATTC TAGTCCTCTG CTGCAGTTCG
GAGGCCAAGT GCGCCAGCGG TATCTGTATA CTGATGATGC TCAGCAGACAGAAGCTCATC TGGAAATTCG
CGAGGACGGC ACAGTGGGAG GCGCTGCTGA TCAGAGCCCA GAAAGCCTGC TGCAGCTGAA
AGCTCTGAAA CCTGGCGTGATCCAGATTCT GGGAGTGAAA ACATCCCGCT TTCTGTGTCA GCGCCCCGAT
GGCGCTCTGT ACGGCTCTCT GCACTTCGAC CCCGAAGCCT GCTCCTTCCGGGAACTGCTG CTGGAAGATG
GGTATAATGT GTATCAGAGC GAAGCCCATG GACTGCCTCT GCATCTGCCC GGCAACAAAT
CCCCCCATAG GGACCCTGCCCCAAGGGGAC CAGCTAGATT TCTGCCTCTG CCCGGCCTGC CACCAGCTCC
ACCAGAACCT CCAGGCATTC TGGCACCTCA GCCCCCAGAC GTGGGAAGCTCTGACCCTCT GTCTATGGTG
GGCCCCTCTC AGGGCAGATC TCCCAGCTAC GCCAGCTAAT GA

(SEQ ID NO: 69)

Exenatide-GG-ABD-GG-FGF21 (DNA-sequence)
(GG-ABD-GG = linker)

CACGGCGAGGGCACCTTCACCAGCGACCTGAGCAAGCAGATGGAGGAGGAGGCCGTGAGACTGTTCATCGAGTGG
CTGAAGAACGGCGGCCCCAGCAGCGGCGCCCCCCCCCCCAGCGGCGGCCTGGCCGAGGCCAAGGTGCTGGCCAAC
AGAGAGCTGGACAAGTACGGCGTGAGCGACTACTACAAGAACCTGATCAACAACGCCAAGACCGTGGAGGGCGTG
AAGGCCCTGATCGACGAGATCCTGGCCGCCCTGCCCGGCGGCCACCCCATCCCCGACAGCAGCCCCCTGCTGCAG
TTCGGCGGCCAGGTGAGACAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAGGCCCACCTGGAGATCAGA
GAGGACGGCACCGTGGGCGGCGCCGCCGACCAGAGCCCCGAGAGCCTGCTGCAGCTGAAGGCCCTGAAGCCCGGC
GTGATCCAGATCCTGGGCGTGAAGACCAGCAGATTCCTGTGCCAGAGACCCGACGGCGCCCTGTACGGCAGCCTG
CACTTCGACCCCGAGGCCTGCAGCTTCAGAGAGCTGCTGCTGGAGGACGGCTACAACGTGTACCAGAGCGAGGCC
CACGGCCTGCCCCTGCACCTGCCCGGCAACAAGAGCCCCCACAGAGACCCCGCCCCCAGAGGCCCCGCCAGATTC
CTGCCCCTGCCCGGCCTGCCCCCCGCCCCCCCCGAGCCCCCCGGCATCCTGGCCCCCCAGCCCCCCGACGTGGGC
AGCAGCGACCCCCTGAGCATGGTGGGCCCCAGCCAGGGCAGAAGCCCCAGCTACGCCAGC

(SEQ ID NO: 70)

Exenatide-FGF21-GG-ABD (DNA-Sequence)
(GG-ABD = linker)
CACGGCGAGGGCACCTTCACCAGCGACCTGAGCAAGCAGATGGAGGAGGAGGCCGTGAGACTGTTCATCGAGTGG
CTGAAGAACGGCGGCCCCAGCAGCGGCGCCCCCCCCCCCAGCCACCCCATCCCCGACAGCAGCCCCCTGCTGCAG
TTCGGCGGCCAGGTGAGACAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAGGCCCACCTGGAGATCAGA
GAGGACGGCACCGTGGGCGGCGCCGCCGACCAGAGCCCCGAGAGCCTGCTGCAGCTGAAGGCCCTGAAGCCCGGC
GTGATCCAGATCCTGGGCGTGAAGACCAGCAGATTCCTGTGCCAGAGACCCGACGGCGCCCTGTACGGCAGCCTG
CACTTCGACCCCGAGGCCTGCAGCTTCAGAGAGCTGCTGCTGGAGGACGGCTACAACGTGTACCAGAGCGAGGCC
CACGGCCTGCCCCTGCACCTGCCCGGCAACAAGAGCCCCCACAGAGACCCCGCCCCCAGAGGCCCCGCCAGATTC
CTGCCCCTGCCCGGCCTGCCCCCCGCCCCCCCCCGAGCCCCCCCGGCATCCTGGCCCCCCAGCCCCCCGACGTGGGC
AGCAGCGACCCCCTGAGCATGGTGGGCCCCAGCCAGGGCAGAAGCCCCAGCTACGCCAGCGGCGGCCTGGCCGAG
GCCAAGGTGCTGGCCAACAGAGAGCTGGACAAGTACGGCGTGAGCGACTACTACAAGAACCTGATCAACAACGCC
AAGACCGTGGAGGGCGTGAAGGCCCTGATCGACGAGATCCTGGCCGCCCTGCCC

(SEQ ID NO: 71)

Exenatide-FGF21-GG-ABD-GG-FGF21 (DNA sequence)
(GG-ABD-GG = linker)

CACGGCGAGGGCACCTTCACCAGCGACCTGAGCAAGCAGATGGAGGAGGAGGCCGTGAGACTGTTCATCGAGTGG
CTGAAGAACGGCGGCCCCAGCAGCGGCGCCCCCCCCCCCAGCCACCCCATCCCCGACAGCAGCCCCCTGCTGCAG
TTCGGCGGCCAGGTGAGACAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAGGCCCACCTGGAGATCAGA
GAGGACGGCACCGTGGGCGGCGCCGCCGACCAGAGCCCCGAGAGCCTGCTGCAGCTGAAGGCCCTGAAGCCCGGC
GTGATCCAGATCCTGGGCGTGAAGACCAGCAGATTCCTGTGCCAGAGACCCGACGGCGCCCTGTACGGCAGCCTG
CACTTCGACCCCGAGGCCTGCAGCTTCAGAGAGCTGCTGCTGGAGGACGGCTACAACGTGTACCAGAGCGAGGCC
CACGGCCTGCCCCTGCACCTGCCCGGCAACAAGAGCCCCCACAGAGACCCCGCCCCCAGAGGCCCCGCCAGATTC
CTGCCCCTGCCCGGCCTGCCCCCCGCCCCCCCCGAGCCCCCCGGCATCCTGGCCCCCCAGCCCCCCGACGTGGGC
AGCAGCGACCCCCTGAGCATGGTGGGCCCCAGCCAGGGCAGAAGCCCCAGCTACGCCAGCGGCGGCCTGGCCGAG
GCCAAGGTGCTGGCCAACAGAGAGCTGGACAAGTACGGCGTGAGCGACTACTACAAGAACCTGATCAACAACGCC
AAGACCGTGGAGGGCGTGAAGGCCCTGATCGACGAGATCCTGGCCGCCCTGCCCGGCGGCCACCCCATCCCCGAC
AGCAGCCCCCTGCTGCAGTTCGGCGGCCAGGTGAGACAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAG
GCCCACCTGGAGATCAGAGAGGACGGCACCGTGGGCGGCGCCGCCGACCAGAGCCCCGAGAGCCTGCTGCAGCTG
AAGGCCCTGAAGCCCGGCGTGATCCAGATCCTGGGCGTGAAGACCAGCAGATTCCTGTGCCAGAGACCCGACGGC
GCCCTGTACGGCAGCCTGCACTTCGACCCCGAGGCCTGCAGCTTCAGAGAGCTGCTGCTGGAGGACGGCTACAAC
GTGTACCAGAGCGAGGCCCACGGCCTGCCCCTGCACCTGCCCGGCAACAAGAGCCCCCACAGAGACCCCGCCCCC
AGAGGCCCCGCCAGATTCCTGCCCCTGCCCGGCCTGCCCCCCGCCCCCCCCGAGCCCCCCGGCATCCTGGCCCCC
CAGCCCCCCGACGTGGGCAGCAGCGACCCCCTGAGCATGGTGGGCCCCAGCCAGGGCAGAAGCCCCAGCTACGCC
AGC

(SEQ ID NO: 72)

Exenatide-GGGGS-His-GGGGS-FGF21 (DNA sequence)
(GGGGS-His-GGGGS = linker)

CACGGCGAG GGCACCTTCA CCAGCGACCT GAGCAAGCAG ATGGAAGAGG AAGCCGTGCG
GCTGTTCATCGAGTGGCTGA AGAATGGCGG CCCTAGCTCT GGCGCCCCTC CACCTTCTGG CGGCGGAGGA
TCTCATGCCC ACGGACACGG ACATGCTCAT GGCGGAGGCGGCTCTCACCC CATCCCTGAT AGTAGCCCCC
TGCTGCAGTT TGGCGGACAA GTGCGGCAGA GATACCTGTA CACCGACGAC GCCCAGCAGA
CCGAGGCCCACCTGGAAATC AGAGAAGATG GCACCGTGGG CGGAGCCGCC GATCAGTCTC CTGAATCTCT
GCTGCAGCTG AAGGCCCTGA AGCCCGGCGT GATCCAGATCCTGGGCGTGA AAACCAGCCG GTTCCTGTGC
CAGAGGCCTG ACGGCGCCCT GTATGGCAGC CTGCACTTTG ATCCTGAGGC CTGCAGCTTC
AGAGAGCTGCTGCTGGAGGA CGGCTACAAC GTGTACCAGT CTGAGGCCCA CGGCCTGCCC CTGCATCTGC
CTGGAAACAA GAGCCCCCAC AGAGATCCCG CCCCTAGAGGCCCTGCCAGA TTCCTGCCAC TGCCTGGACT
GCCTCCAGCC CCTCCTGAGC CTCCTGGAAT TCTGGCTCCC CAGCCTCCTG ATGTGGGCAG
CAGCGATCCTCTGAGCATGG TGGGACCTAG CCAGGGCAGA AGCCCTAGCT ACGCCAGCTA A

(SEQ ID NO: 73)

Exenatide-GGGGS-His-GGGGS-ABD-GG-FGF21 (DNA sequence)
(GGGGS-His-GGGGS-ABD-GG = linker)

CACGGCGAG GGCACCTTCA CCAGCGACCT GAGCAAGCAG ATGGAAGAGG AAGCCGTGCG
GCTGTTCATCGAGTGGCTGA AGAATGGCGG CCCTAGCTCT GGCGCCCCTC CACCTTCTGG CGGCGGAGGA
TCTCATGCCC ACGGACACGG ACATGCTCAT GGCGGAGGCGGATCTCTGGC CGAGGCTAAG GTGCTGGCCA
ACAGAGAGCT GGATAAGTAC GGCGTGTCCG ACTACTACAA GAACCTGATC AACAACGCCA
AGACCGTGGAAGGCGTGAAG GCCCTGATCG ACGAGATTCT GGCTGCCCTG CCTGGCGGCC ACCCTATCCC
TGATTCAAGC CCCCTGCTGC AGTTCGGCGG ACAAGTGCGGCAGAGATACC TGTACACCGA CGACGCCCAG
CAGACCGAGG CCCACCTGGA AATCAGAGAA GATGGCACCG TGGGCGGAGC CGCCGATCAG
TCTCCTGAATCTCTGCTGCA GCTGAAAGCC CTGAAGCCCG GCGTGATCCA GATCCTGGGC GTGAAAACCA
GCCGGTTCCT GTGCCAGAGG CCTGACGGCG CCCTGTATGGCAGCCTGCAC TTTGATCCTG AGGCCTGCAG
CTTTAGAGAG CTGCTGCTGG AGGACGGCTA CAACGTGTAC CAGTCTGAGG CCCACGGCCT
GCCCCTGCATCTGCCTGGAA ACAAGAGCCC CCACAGAGAT CCCGCCCCTA GAGGCCCTGC CAGATTCCTG
CCTCTGCCCG GACTGCCTCC TGCCCCTCCT GAACCTCCTGGAATTCTGGC CCCCCAGCCT CCTGATGTGG
GCAGCTCTGA TCCCCTGAGC ATGGTGGGAC CTAGCCAGGG CAGAAGCCCT AGCTACGCCA GCTAA

(SEQ ID NO: 74)

Exenatide-GG-Cys-$(G)_{21}$-FGF21 (GG-Cys-$(G)_{21}$ = linker) (DNA sequence)

CACGGCGAGGGCACCTTCACCAGCGACCTGAGCAAGCAGATGGAGGAGGAGGCCGTGAGACTGTTCATCGAGTGG
CTGAAGAACGGCGGCCCCAGCAGCGGCGCCCCCCCCCCCAGCGGCGGCTGCGGCGGCGGCGGCGGCGGCGGC
GGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCACCCCATCCCCGACAGCAGCCCCCTGCTGCAGTTCGGC
GGCCAGGTGAGACAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAGGCCCACCTGGAGATCAGAGAGGAC
GGCACCGTGGGCGGCGCCGCCGACCAGAGCCCCGAGAGCCTGCTGCAGCTGAAGGCCCTGAAGCCCGGCGTGATC
CAGATCCTGGGCGTGAAGACCAGCAGATTCCTGTGCCAGAGACCCGACGGCGCCCTGTACGGCAGCCTGCACTTC
GACCCCGAGGCCTGCAGCTTCAGAGAGCTGCTGCTGGAGGACGGCTACAACGTGTACCAGAGCGAGGCCCACGGC
CTGCCCCTGCACCTGCCCGGCAACAAGAGCCCCCACAGAGACCCCGCCCCCAGAGGCCCCGCCAGATTCCTGCCC
CTGCCCGGCCTGCCCCCCGCCCCCCCCGAGCCCCCCGGCATCCTGGCCCCCCAGCCCCCCGACGTGGGCAGCAGC
GACCCCCTGAGCATGGTGGGCCCCAGCCAGGGCAGAAGCCCCAGCTACGCCAGC

(SEQ ID NO: 75)

Exenatide-GG-Lys-$(G)_{21}$-FGF21 (GG-Lys-$(G)_{21}$ = linker) (DNA sequence)

CACGGCGAGGGCACCTTCACCAGCGACCTGAGCAAGCAGATGGAGGAGGAGGCCGTGAGACTGTTCATCGAGTGG
CTGAAGAACGGCGGCCCCAGCAGCGGCGCCCCCCCCCCCAGCGGCGGCAAGGGCGGCGGCGGCGGCGGCGGC
GGCAGCGGCGGCGGCGGCAGCGGCGGCGGCGGCAGCCACCCCATCCCCGACAGCAGCCCCCTGCTGCAGTTCGGC
GGCCAGGTGAGACAGAGATACCTGTACACCGACGACGCCCAGCAGACCGAGGCCCACCTGGAGATCAGAGAGGAC
GGCACCGTGGGCGGCGCCGCCGACCAGAGCCCCGAGAGCCTGCTGCAGCTGAAGGCCCTGAAGCCCGGCGTGATC
CAGATCCTGGGCGTGAAGACCAGCAGATTCCTGTGCCAGAGACCCGACGGCGCCCTGTACGGCAGCCTGCACTTC
GACCCCGAGGCCTGCAGCTTCAGAGAGCTGCTGCTGGAGGACGGCTACAACGTGTACCAGAGCGAGGCCCACGGC
CTGCCCCTGCACCTGCCCGGCAACAAGAGCCCCCACAGAGACCCCGCCCCCAGAGGCCCCGCCAGATTCCTGCCC
CTGCCCGGCCTGCCCCCCGCCCCCCCCGAGCCCCCCGGCATCCTGGCCCCCCAGCCCCCCGACGTGGGCAGCAGC
GACCCCCTGAGCATGGTGGGCCCCAGCCAGGGCAGAAGCCCCAGCTACGCCAGC

(SEQ ID NO: 76)

Exenatide-GG-IgG 1 Asp103-Lys329-GG-FGF21 (GG-IgG 1 Asp103-Lys329-GG = linker) (DNA sequence)

CATGGTGAAGGCACCT TTACCAGCGA TCTGAGCAAA CAAATGGAAG AAGAAGCAGT TCGCCTGTTT
ATTGAATGGC TGAAAAATGG TGGTCCGAGC AGTGGTGCACCGCCTCCGAG TGGTGGTGAT AAAACCCATA
CCTGTCCGCC TTGTCCGGCT CCGGAACTGC TGGGTGGTCC GTCAGTTTTT CTGTTTCCGC
CTAAACCGAAAGATACCCTG ATGATTAGCC GTACACCGGA AGTGACCTGT GTTGTTGTTG ATGTTAGCCA
TGAAGATCCT GAGGTGAAAT TTAACTGGTA TGTTGATGGTGTGGAAGTGC ATAATGCAAA AACAAAACCG
CGTGAGGAAC AGTATAATTC AACCTATCGT GTTGTTAGCG TTCTGACCGT TCTGCATCAG
GATTGGCTGAATGGTAAAGA ATACAAATGC AAAGTGAGCA ACAAAGCACT GCCTGCACCG ATTGAAAAAA
CCATTAGCAA AGCAAAAGGT CAGCCTCGTG AACCGCAGGTTTATACCCTG CCTCCGAGCC GTGATGAACT
GACCAAAAAT CAGGTTAGCC TGACCTGTCT GGTGAAAGGT TTTTATCCGA GCGATATTGC
AGTTGAATGGGAAAGCAATG GTCAGCCGGA AAATAACTAT AAAACCACCC CTCCGGTTCT GGATAGTGAT
GGTAGCTTTT TCCTGTATAG CAAACTGACC GTTGATAAAAGCCGTTGGCA GCAGGGTAAT GTTTTTAGCT
GTAGCGTTAT GCATGAAGCC CTGCATAATC ATTATACCCA GAAAAGCCTG AGCCTGAGTC
CGGGTAAAGGCGGTCATCCG ATTCCGGATA GCAGTCCGCT GCTGCAGTTT GGTGGCCAGG TTCGTCAGCG
TTATCTGTAT ACCGATGATG CACAGCAGAC CGAAGCCCATCTGGAAATTC GTGAAGATGG CACCGTTGGT
GGTGCAGCAG ATCAGAGTCC GGAAAGCCTG CTGCAGCTGA AAGCACTGAA ACCGGGTGTT
ATTCAGATTCTGGGTGTTAA AACCAGCCGC TTTCTGTGTC AGCGTCCGGA TGGTGCACTG TATGGTAGTC
TGCATTTTGA TCCGGAAGCA TGTAGCTTTC GTGAACTGCTGCTGGAAGAT GGTTATAATG TTTATCAGAG
CGAAGCGCAT GGTCTGCCGC TGCATCTGCC TGGTAATAAA AGTCCGCATC GTGATCCGGC
ACCGCGTGGTCCGGCACGTT TTCTGCCTCT GCCAGGTCTG CCTCCGGCAC CTCCTGAACC GCCTGGTATT
CTGGCACCGC

(SEQ ID NO: 77)

Exenatide-GG-IgG1 Pro120-Lys329-GG-FGF21 (GG-IgG1 Pro120-Lys329-GG = linker) (DNA sequence)

CATGGTGAAGGCACCT TTACCAGCGA TCTGAGCAAA CAAATGGAAG AAGAAGCAGT TCGCCTGTTT
ATTGAATGGC TGAAAAATGG TGGTCCGAGC AGTGGTGCACCGCCTCCGTC AGGTGGTCCG TCAGTTTTTC
TGTTTCCGCC TAAACCGAAA GATACCCTGA TGATTAGCCG TACACCGGAA GTGACCTGTG
TTGTTGTTGATGTTAGCCAT GAAGATCCTG AGGTGAAATT TAACTGGTAT GTTGATGGTG TGGAAGTGCA
TAATGCAAAA ACAAAACCGC GTGAGGAACA GTATAATTCAACCTATCGTG TTGTTAGCGT TCTGACCGTT
CTGCATCAGG ATTGGCTGAA TGGTAAAGAA TACAAATGCA AAGTGAGCAA CAAAGCACTG
CCTGCACCGATTGAAAAAAC CATTAGCAAA GCAAAAGGTC AGCCTCGTGA ACCGCAGGTT TATACCCTGC
CTCCGAGCCG TGATGAACTG ACCAAAAATC AGGTTAGCCTGACCTGTCTG GTGAAAGGTT TTTATCCGAG
CGATATTGCA GTTGAATGGG AAAGCAATGG TCAGCCGGAA AATAACTATA AAACCACCCC
TCCGGTTCTGGATAGTGATG GTAGCTTTTT CCTGTATAGC AAACTGACCG TTGATAAAAG CCGTTGGCAG
CAGGGTAATG TTTTTAGCTG TAGCGTTATG CATGAAGCCCTGCATAATCA TTATACCCAG AAAAGCCTGA
GCCTGAGTCC GGGTAAAGGC GGTCATCCGA TTCCGGATAG CAGTCCGCTG CTGCAGTTTG
GTGGCCAGGTTCGTCAGCGT TATCTGTATA CCGATGATGC ACAGCAGACC GAAGCCCATC TGGAAATTCG
TGAAGATGGC ACCGTTGGTG GTGCAGCAGA TCAGAGTCCGGAAAGCCTGC TGCAGCTGAA AGCACTGAAA
CCGGGTGTTA TTCAGATTCT GGGTGTTAAA ACCAGCCGCT TTCTGTGTCA GCGTCCGGAT
GGTGCACTGTATGGTAGTCT GCATTTTGAT CCGGAAGCAT GTAGCTTTCG TGAACTGCTG CTGGAAGATG
GTTATAATGT TTATCAGAGC GAAGCGCATG GTCTGCCGCTGCATCTGCCT GGTAATAAAA GTCCGCATCG
TGATCCGGCA CCGCGTGGTC CGGCACGTTT TCTGCCTCTG CCAGGTCTGC CTCCGGCACC
TCCTGAACCGCCTGGTATTC TGGCACCGCA GCCTCCGGAT GTTGGTAGCA GCGATCCGCT GAGCATGGTG
GGTCCGTCAC AGGGTCGTAG CCCGAGCTAT GCAAGCTAA

(SEQ ID NO: 78)

Exenatide-GG-IgG1 Pro120-Lys329 mutated-GG-FGF21 (GG-IgG1 Pro120-Lys329 mutated-GG = linker) (DNA sequence)

CATGGTGAAGGCACCT TTACCAGCGA TCTGAGCAAA CAAATGGAAG AAGAAGCAGT TCGCCTGTTT
ATTGAATGGC TGAAAAATGG TGGTCCGAGC AGTGGTGCACCGCCTCCGTC AGGTGGTCCG TCAGTTTTTC
TGTTTCCGCC TAAACCGAAA GATACCCTGA TGATTAGCCG TACACCGGAA GTGACCTGTG
TTGTTGTTGATGTTAGCCAT GAAGATCCTG AGGTGAAATT TAACTGGTAT GTTGATGGTG TGGAAGTGCA
TAATGCAAAA ACAAAACCGC GTGAGGAACA GTATAATTCAACCTATCGTG TTGTTAGCGT TCTGACCGTT
CTGCATCAGG ATTGGCTGAA TGGTAAAGAA TACAAATGCA AAGTGAGCAA CAAAGCACTG
CCTGCACCGATTGAAAAAAC CATTAGCAAA GCAAAAGGTC AGCCTCGTGA ACCGCAGGTT TATACCAGCC
CTCCGAGCCG TGATGAACTG ACCAAAAATC AGGTTAGTCTGCGTTGTCAT GTGAAAGGTT TTTATCCGAG
CGATATTGCA GTTGAATGGG AAAGCAATGG TCAGCCGGAA AATAACTATA AAACCACCAA
ACCGGTTCTGGATTCAGATG GTTCATTTGA ACTGAAAAGC GCACTGACCG TTGATAAAAG CCGTTGGCAG
CAGGGTAATG TTTTTAGCTG TAGCGTTATG CATGAAGCCCTGCATAATCA TTATACCCAG AAAAGCCTGA
GCCTGAGTCC GGGTAAAGGC GGTCATCCGA TTCCGGATAG CAGTCCGCTG CTGCAGTTTG
GTGGCCAGGTTCGTCAGCGT TATCTGTATA CCGATGATGC ACAGCAGACC GAAGCCCATC TGGAAATTCG
TGAAGATGGC ACCGTTGGTG GTGCAGCAGA TCAGAGTCCGGAAAGCCTGC TGCAGCTGAA AGCACTGAAA
CCGGGTGTTA TTCAGATTCT GGGTGTTAAA ACCAGCCGCT TTCTGTGTCA GCGTCCGGAT
GGTGCACTGTATGGTAGTCT GCATTTTGAT CCGGAAGCAT GTAGCTTTCG TGAACTGCTG CTGGAAGATG
GTTATAATGT TTATCAGAGC GAAGCGCATG GTCTGCCGCTGCATCTGCCT GGTAATAAAA GTCCGCATCG
TGATCCGGCA CCGCGTGGTC CGGCACGTTT TCTGCCTCTG CCAGGTCTGC CTCCGGCACC
TCCTGAACCGCCTGGTATTC TGGCACCGCA GCCTCCGGAT GTTGGTAGCA GCGATCCGCT GAGCATGGTG
GGTCCGTCAC AGGGTCGTAG CCCGAGCTAT GCAAGCTAA

(SEQ ID NO: 103)

Exenatide-GG-IgG1 Pro120-Lys222-GG-FGF21 (GG-IgG1 Pro120-Lys222-GG = linker) (DNA sequence)

CATGGTGAAGGCACCT TTACCAGCGA TCTGAGCAAA CAAATGGAAG AAGAAGCAGT TCGCCTGTTT
ATTGAATGGC TGAAAAATGG TGGTCCGAGC AGTGGTGCACCGCCTCCGTC AGGTGGTCCG TCAGTTTTTC
TGTTTCCGCC TAAACCGAAA GATACCCTGA TGATTAGCCG TACACCGGAA GTGACCTGTG
TTGTTGTTGATGTTAGCCAT GAAGATCCTG AGGTGAAATT TAACTGGTAT GTTGATGGTG TGGAAGTGCA
TAATGCAAAA ACAAAACCGC GTGAGGAACA GTATAATTCAACCTATCGTG TTGTTAGCGT TCTGACCGTT
CTGCATCAGG ATTGGCTGAA TGGTAAAGAA TACAAATGCA AAGTGAGCAA CAAAGCACTG
CCTGCACCGATTGAAAAAAC CATTAGCAAA GCAAAAGGTG GTCATCCGAT TCCGGATAGC AGTCCGCTGC
TGCAGTTTGG TGGCCAGGTT CGTCAGCGTT ATCTGTATACCGATGATGCA CAGCAGACCG AAGCCCATCT
GGAAATTCGT GAAGATGGCA CCGTTGGTGG TGCAGCAGAT CAGAGTCCGG AAAGCCTGCT
GCAGCTGAAAGCACTGAAAC CGGGTGTTAT TCAGATTCTG GGTGTTAAAA CCAGCCGCTT TCTGTGTCAG
CGTCCGGATG GTGCACTGTA TGGTAGTCTG CATTTTGATCCGGAAGCATG TAGCTTTCGT GAACTGCTGC
TGGAAGATGG TTATAATGTT TATCAGAGCG AAGCGCATGG TCTGCCGCTG CATCTGCCTG
GTAATAAAAGTCCGCATCGT GATCCGGCAC CGCGTGGTCC GGCACGTTTT CTGCCTCTGC CAGGTCTGCC
TCCGGCACCT CCTGAACCGC CTGGTATTCT GGCACCGCAGCCTCCGGATG TTGGTAGCAG CGATCCGCTG
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(SEQ ID NO: 104)

Figure 4

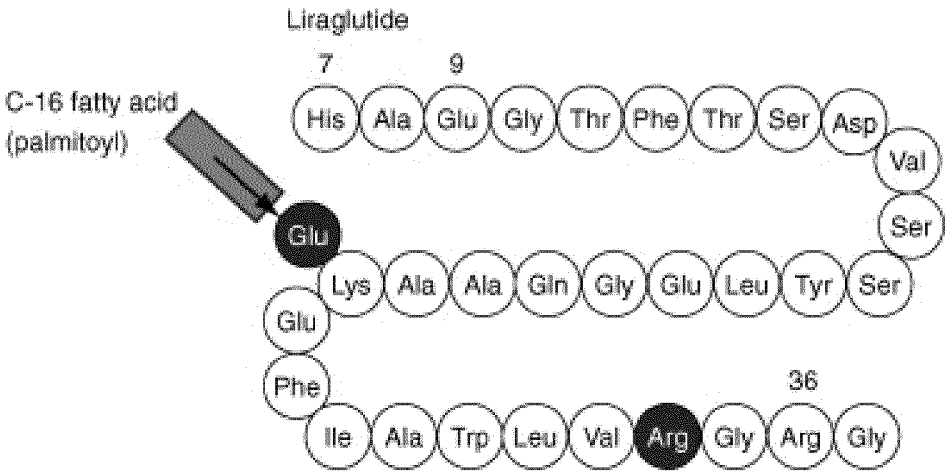

Liraglutide
7
9
C-16 fatty acid
(palmitoyl)
His
Ala
Glu
Gly
Thr
Phe
Thr
Ser
Asp
Val
Ser
Glu
Lys
Ala
Ala
Gln
Gly
Glu
Leu
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Phe
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Leu
Val
Arg
Gly
Arg
Gly

Figure 5

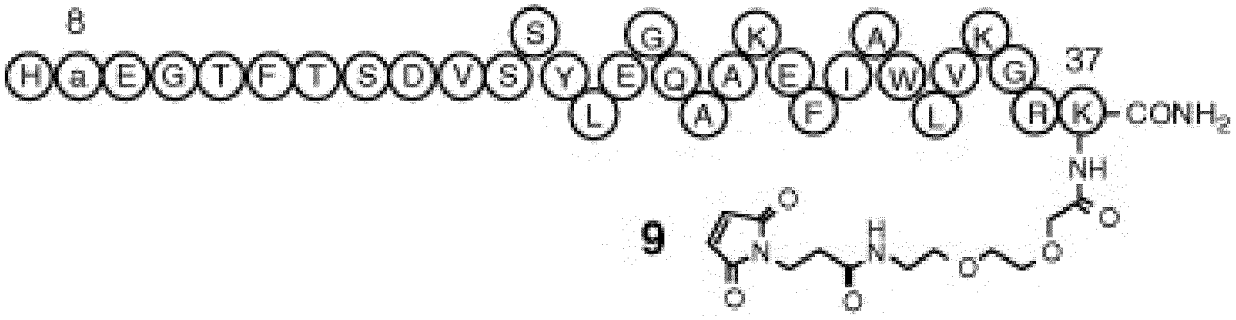


Figure 6

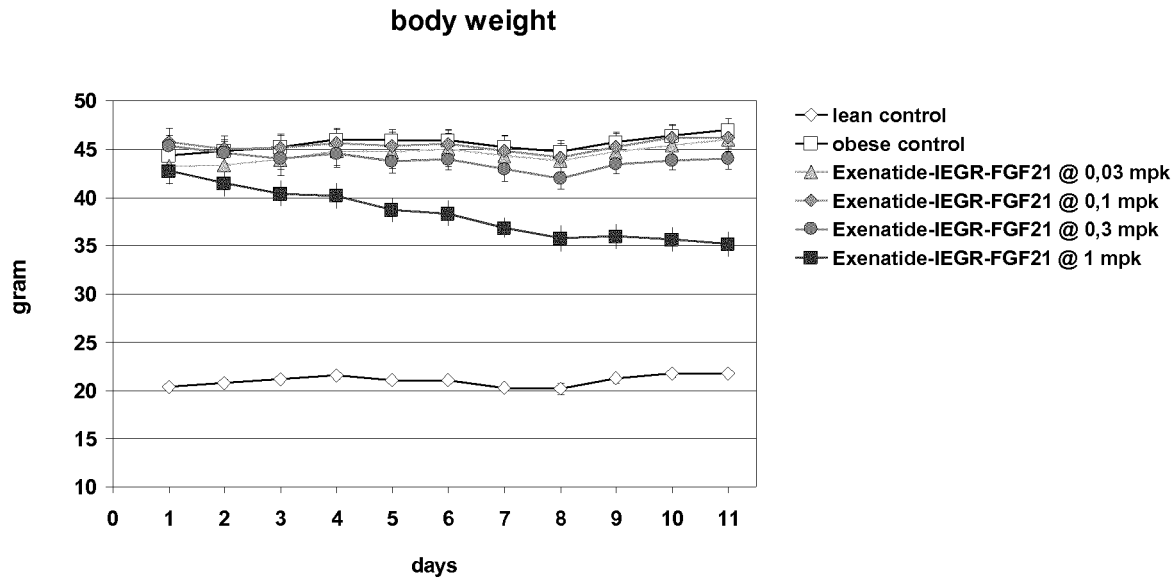


Figure 7

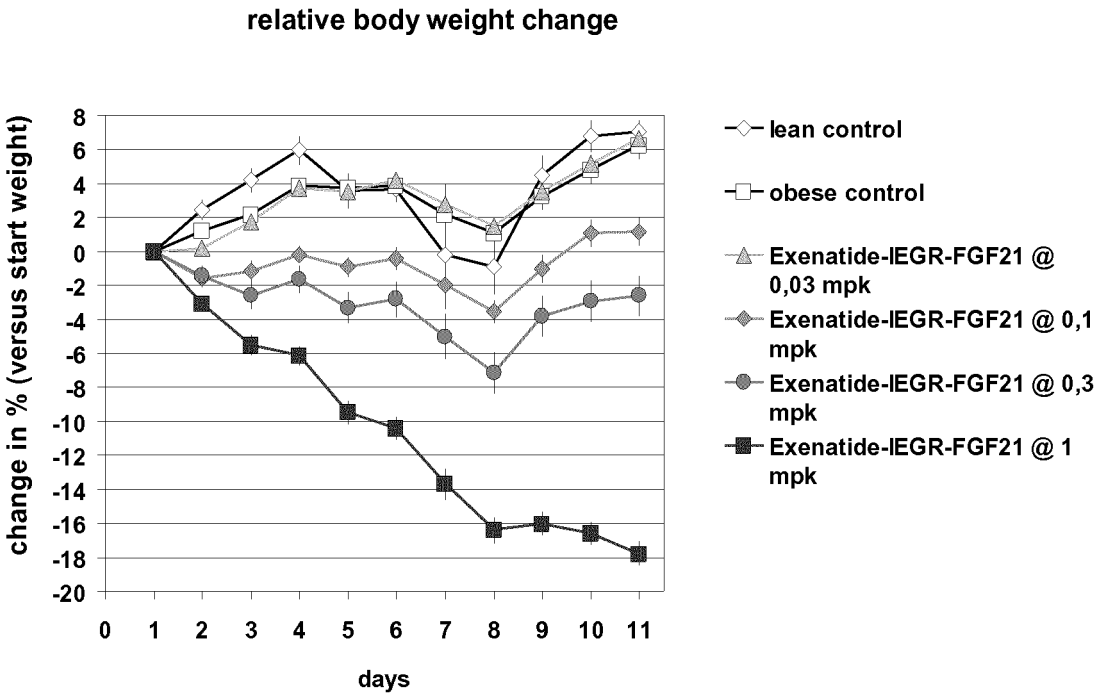


Figure 8

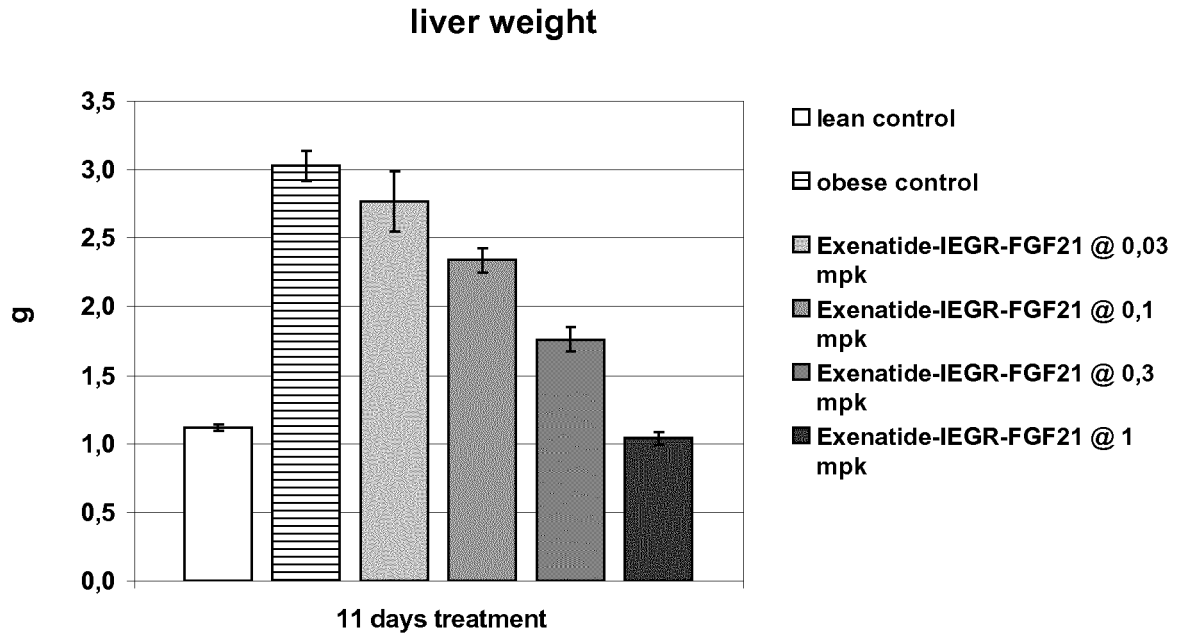


Figure 9

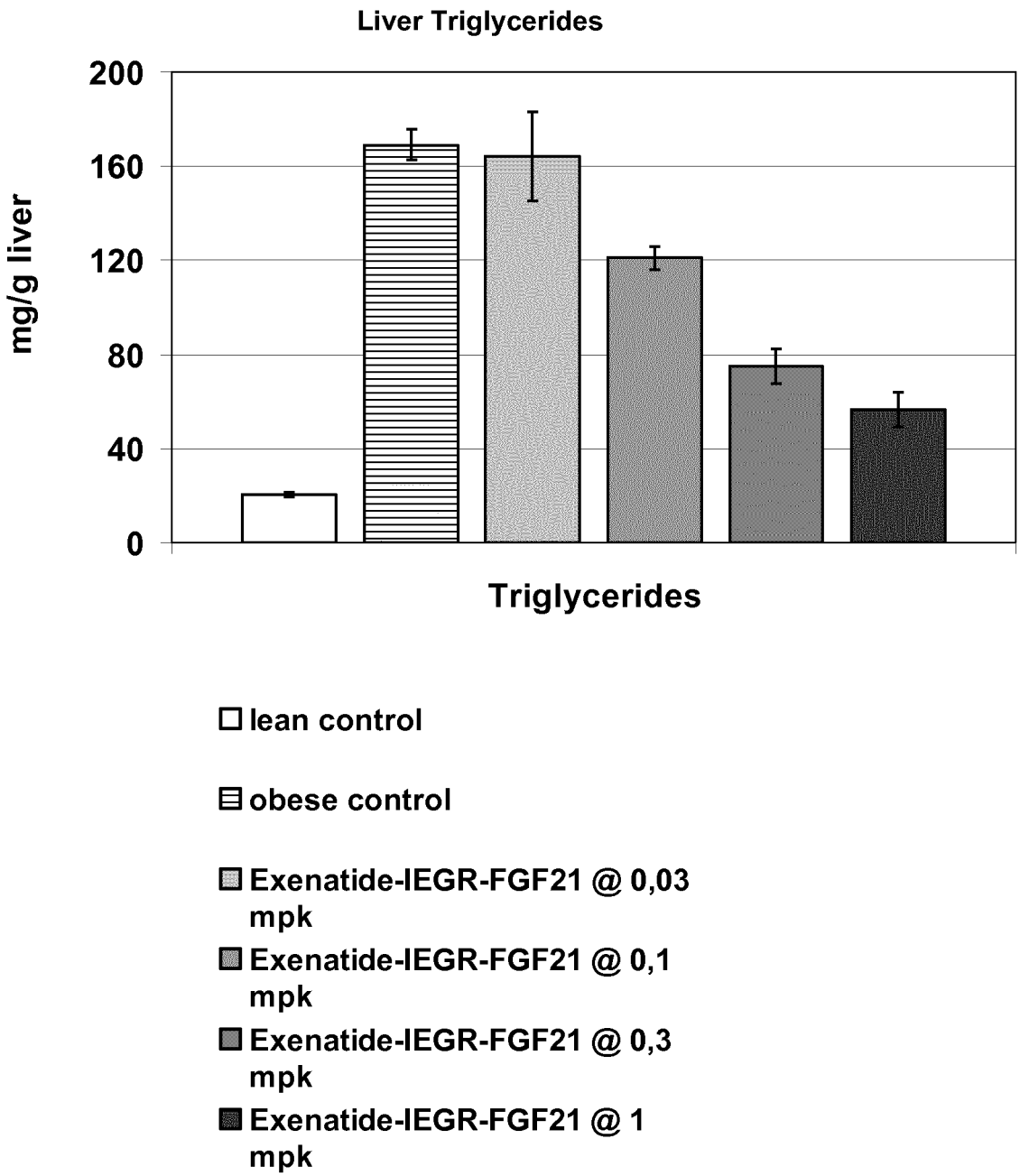

Liver Triglycerides
200
160
120
80
40
0
mg/g liver
Triglycerides
lean control
obese control
Exenatide-IEGR-FGF21 @ 0,03 mpk
Exenatide-IEGR-FGF21 @ 0,1 mpk
Exenatide-IEGR-FGF21 @ 0,3 mpk
Exenatide-IEGR-FGF21 @ 1 mpk

Figure 10

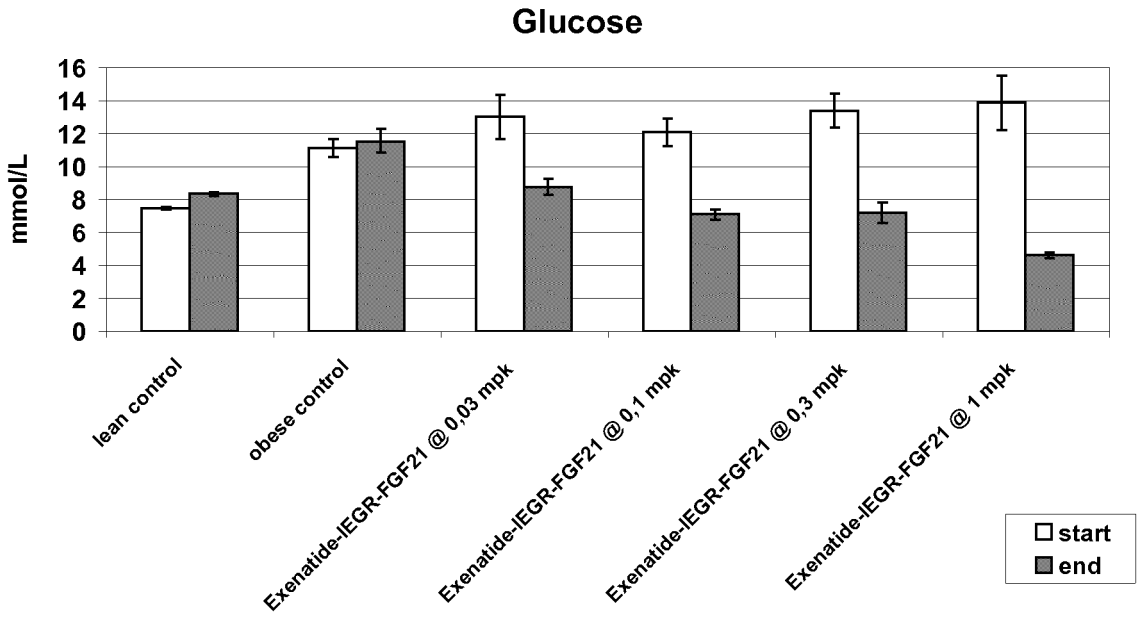


Figure 11

