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(54) G L P -1의 유사체

요약

본 발명은 글루카곤형 펩타이드-1의 펩타이드 유사체, 제약학적으로 허용 가능한 이들의 염, 상기 유사체를 사용하여 포유류를 치료하는 방법 및 이러한 치료방법에 유용한, 상기 유사체를 포함하는 약제 조성물에 관한 것이다.

색인어

글루카곤, 펩타이드, 유사체, 아고니스트 작용, 당뇨병

명세서

발명의 상세한 설명

발명의 목적

발명이 속하는 기술 및 그 분야의 종래기술

본 발명은 글루카곤형 펩타이드-1의 펩타이드 유사체, 제약학적으로 허용 가능한 이들의 염, 상기 유사체를 사용하여 포유류를 치료하는 방법 및 이러한 치료방법에 유용한, 상기 유사체를 포함하는 약제 조성물에 관한 것이다.

글루카곤형 펩타이드-1(7-36) 아미드(GLP-1)는 글루카곤의 전구체인 프리프로글루카곤의 조직 특이적인 번역 후의 프로세싱에 의하여 장의 L-세포 내에서 합성되며(Varndell, J.M., et al., J. Histochem Cytochem, 1985:33:1080-6), 식이에 대한 반응으로서 순환계로 방출된다. GLP-1의 혈장 농도는 공복 시 대략 15 pmol/ℓ의 수준이고 식후에는 40 pmol/ℓ의 수준으로 높아진다. 혈장 포도당 농도의 상승에 있어서, 포도당을 정맥내 투여하는 경우에 비해 경구 투여하는 경우, 혈장 인슐린이 대략 3배 증가되는 것이 제시되어 있다(Kreymann, B., et al., Lancet 1987:2, 1300-4). 인크레틴 효과(incretin effect)로 알려진 인슐린 방출에 있어서의 이러한 식이성 증대는 주로 체액에 의한 것이며, 현재는 GLP-1이 인체 내에서 가장 유력한 생리학적 인크레틴인 것으로 여겨지고 있다. 인슐린성 효과 외에도, GLP-1은 글루카곤 분비를 억제하고, 공복화를 지연시키며(Wettergren A, et al., Dig Dis Sci 1993:38:665-73), 포도당의 말초 분포를 증진할 수 있다(D'Alessio, D.A. et al., J. Clin Invest 1994:93:2293-6).

1994년, GLP-1의 1회 피하(s/c) 투여량이 인슐린 비의존성 당뇨증(NIDDM)을 가진 환자에게 식후의 포도당 수준을 완전히 정상화할 수 있다는 사실이 밝혀진 후, GLP-1의 치료 가능성이 제안되었다(Gutniak, M.K., et al., Diabetes Care 1994:17:1039-44). 이러한 효과는 증가된 인슐린 방출 및 글루카곤 분비에 있어서의 감소 모두에 의해 조절되는 것으로 여겨졌다. 또한, GLP-1의 정맥내 주입은 NIDDM을 가지는 환자에 있어 식후 공복화를 지연시키는 것으로 밝혀졌다(Williams, B., et al., J. Clin Endo Metab 1996:81:327-32). 술포닐우레아와는 달리, GLP-1의 인슐린에 대한 작용은 혈장의 포도당 농도에 의존한다(Holz, G.G. 4th, et al., Nature 1993:361:362-5). 따라서, 낮은 혈장 포도당 농도에서 GLP-1에 의해 매개되는 인슐린의 방출 감소는 심한 저혈당증을 방지한다. 이러한 작용을 종합해 보면 현재 NIDDM 치료에 사용되는 다른 제제들을 능가하는 GLP-1만의 독특하고 유력한 치료 효과가 얻어진다.

여러 가지 연구에서, 건강한 대상 내에서 GLP-1은 혈당 수준뿐 아니라 인슐린 및 글루카곤 농도에도 유력한 영향을 미치는 것으로 밝혀졌으며(Orskov, C, Diabetologia 35:701-711, 1992; Holst, J.J., et al., Potential of GLP-1 in diabetes management in Glucagon Ⅲ, Handbook of Experimental Pharmacology, Lefevbre PJ, Ed. Berlin, Springer Verlag, 1996, p. 311-326), 이들 효과는 포도당 의존성임이 밝혀졌다(Kreymann, B., et al., Lancet ii; 1300-1304, 1987; Weir, G.C., et al., Diabetes 38:338-342, 1989). 게다가, GLP-1은 당뇨병 환자들에게도 효과적이며(Gutniak, M., N. Engl J Med 226:1316-1322, 1992; Nathan, D.M., et al., Diabetes Care 15:270-276, 1992), 보다 구체적으로는 II형 당뇨병을 가지는 대상의 경우에는 혈당 수준을 정상화하고(Nauck, M.A., et al., Diagbetologia 36:741-744, 1993), I형 당뇨병 환자의 경우에는 혈당 조절을 개선하며(Creutzfeldt, W.O., et al., Diabetes Care 19:580-586, 1996), 이는 GLP-1의 치료제로서의 사용 가능성을 증대시켰다.

발명이 이루고자 하는 기술적 과제

그러나, GLP-1은 대사적으로 불안정하고, 생체 내에서 단지 1분 내지 2분의 혈장 반감기($t_{1/2}$)를 갖는다. 외부에서 투여되는 GLP-1 또한 빠르게 분해된다(Deacon, C.F., et al., Diabetes 44:1126-1131, 1995). 이러한 대사 불안정성은 천연 GLP-1의 치료제로서의 가능성을 제한한다. 따라서, 천연 GLP-1보다 효과적이고 대사적으로도 보다 안정된 GLP-1 유사체가 요구된다.

발명의 구성 및 작용

제1 양태에서, 본 발명은 하기 화학식(Ⅰ)의 화합물 또는 제약학적으로 허용하능한 이들의 염에 관한 것이다:

(R^2R^3)-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-

A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-A^{39}-R^1 (Ⅰ)

상기 식에서,

A^1은 L-His, Ura, Paa, Pta, Amp, Tma-His 또는 탈아미노(des-amino)-His이거나 결실이고;

A^8은 Ala, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala 또는 N-Me-Gly이고;

A^9는 Glu, N-Me-Glu, N-Me-Asp 또는 Asp이고;

A^{10}은 Gly, Acc, β-Ala 또는 Aib이고;

A^{11}은 Thr 또는 Ser이고;

A^{12}는 Phe, Acc, Aic, Aib, 3-Pal, 4-Pal, β-Nal, Cha, Trp 또는 X^1-Phe이고;

A^{13}은 Thr 또는 Ser이고;

A^{14}는 Ser 또는 Aib이고;

A^{15}는 Asp 또는 Glu이고;

A^{16}은 Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala 또는 Cha이고;

A^{17}은 Ser 또는 Thr이고;

A^{18}은 Ser 또는 Thr이고;

A^{19}는 Tyr, Cha, Phe, 3-Pal, 4-Pal, Acc, β-Nal 또는 X^1-Phe이고;

A^{20}은 Leu, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe 또는 X^1-Phe이고;

A^{21}은 Glu 또는 Asp이고;

A^{22}는 Gly, Acc, β-Ala, Glu 또는 Aib이고;

A^{23}은 Gln, Asp, Asn 또는 Glu이고;

A^{24}는 Ala, Aib, Val, Abu, Tle 또는 Acc이고;

A^{25}는 Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이고;

A^{26}은 Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O))이고;

A^{27}은 Glu, Asp, Leu, Aib 또는 Lys이고;

A^{28}은 Phe, Pal, β-Nal, X^1-Phe, Aic, Acc, Aib, Cha 또는 Trp이고;

A^{29}는 Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala 또는 Phe이고;

A^{30}은 Ala, Aib 또는 Acc이고;

A^{31}은 Trp, β-Nal, 3-Pal, 4-Pal, Phe, Acc, Aib 또는 Cha이고;

A^{32}는 Leu, Acc, Aib, Nle, Ile, Cha, Tle, Phe, X^1-Phe 또는 Ala이고;

A^{33}은 Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, Lys 또는 X^1-Phe이고;

A^{34}는 Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이고;

A^{35}는 Gly, β-Ala, D-Ala, Gaba, Ava, HN-$(CH_2)_m$-C(O), Aib, Acc 또는 D-아미산이고;

A^{36}은 L- 또는 D-Arg, D- 또는 L-Lys, D- 또는 L-hArg, D- 또는 L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$)-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이거나 결실이고;

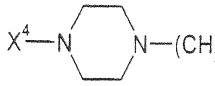
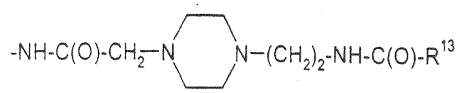
A^{37}은 Gly, β-Ala, Gaba, Ava, Aib, Acc, Ado, Arg, Asp, Aun, Aec, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O) 또는 D-아미노산이거나 결실이고;

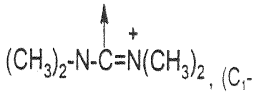
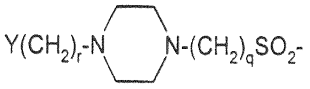
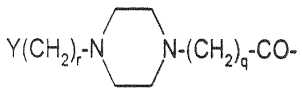
A^{38}은 D- 또는 L-Lys, D- 또는 L-Arg, D- 또는 L-hArg, D- 또는 L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O), Ava, Ado 또는 Aec이거나 결실이고;

A^{39}는 D- 또는 L-Lys, D- 또는 L-Arg, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), Ava, Ado, 또는 Aec이고;

각각의 경우에 대하여 X^1은 (C_1-C_6)알킬, OH 및 할로(halo)기로 이루어지는 군으로부터 독립적으로 선택되고;

R^1은 OH, NH_2, (C_1-C_{30})알콕시 및 NH-X^2-CH_2-Z^0이고, 여기서 X^2는 (C_1-C_{12})탄화수소 모이어티이고, Z^0은 H, OH, $C0_2H$ 및 $CONH_2$로 이루어지는 군으로부터 선택되고;

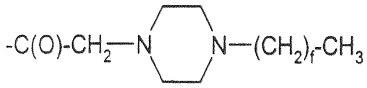
X^3은  ,  및 $-C(O)-NHR^{12}$로 이루어지는 군으로부터 선택되며, 여기서 X^4는 각각의 경우에 대하여 -C(O)-, -NH-C(O)- 및 $-CH_2-$으로 이루어지는 군으로부터 독립적으로 선택되고, f는 각각의 경우에 대해 독립적으로 1 내지 29를 포함하는 정수 중 하나이고;

각각의 R^2 및 R^3은 H, (C_1-C_{30})알킬, (C_2-C_{30})알케닐, 페닐(C_1-C_{30})알킬, 나프틸(C_1-C_{30})알킬, 하이드록시(C_1-C_{30})알킬, 하이드록시(C_2-C_{30})알케닐, 하이드록시페닐(C_1-C_{30})알킬 및 하이드록시나프틸(C_1-C_{30})알킬로 이루어지는 군으로부터 독립적으로 선택되거나; R^2와 R^3 중 하나는 , (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, $C(O)X^5$,  및  로 이루어지는 군으로부터 선택되며; 상기 식에서 Y는 H, OH 및 NH_2로 이루어지는 군으로부터 선택되고; r은 0 내지 4이고; q는 0 내지 4이고; X^5는 (C_1-C_{30})알킬, (C_2-C_{30})알케닐, 페닐(C_1-C_{30})알킬, 나프틸(C_1-C_{30})알킬, 하이드록시(C_1-C_{30})알킬, 하이드록시(C_2-C_{30})알케닐, 하이드록시페닐(C_1-C_{30})알킬 및 하이드록시나프틸(C_1-C_{30})알킬로 이루어지는 군으로부터 선택되고;

e는 각각의 경우에 대하여 독립적으로 1 내지 4를 포함하는 정수 중 하나이고;

m은 각각의 경우에 대하여 독립적으로 5 내지 24를 포함하는 정수 중 하나이고;

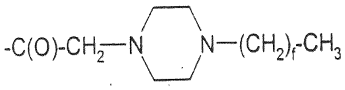
n은 각각의 경우에 대하여 독립적으로 1 내지 5를 포함하는 정수 중 하나이고;

R^{10} 및 R^{11} 각각은 각각의 경우에 대하여 H, (C_1-C_{30})알킬, (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, -C((NH)(NH_2)) 및  으로 이루어지는 군으로부터 독립적으로 선택되고;

R^{12} 및 R^{13} 각각은 각각의 경우에 대하여 독립적으로 (C_1-C_{30})알킬이고;

단,

A^7이 Ura, Paa 또는 Pta인 경우, R^2 및 R^3은 결실이고;

R^{10}이 (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, -C((NH)(NH_2)) 및  로 이루어지는 군으로부터 선택되는 경우, R^{11}은 H 또는 (C_1-C_{30})알킬이고;

(i) 화학식(Ⅰ)의 화합물 중 적어도 하나의 아미노산은 hGLP-1(7-36, -37 또는 -38)NH_2 또는 hGLP-1(7-36, -37 및 -38)OH의 천연 서열과 동일하지 않고;

(ii) 화학식(Ⅰ)의 화합물은 hGLP-1(7-36, -37 또는 -38)NH_2 또는 hGLP-1(7-36, -37 또는 -38)OH—여기서 한 위치가 Ala로 치환됨—의 유사체가 아니고;

(iii) 화학식(Ⅰ)의 화합물은 ($Arg^{26,34}$, Lys^{38})hGLP-1(7-38)-E, (Lys^{26}(N_ε-알카노일))hGLP-1(7-36, -37 또는 -38)-E, (Lys^{34}(N_ε-알카노일))hGLP-1(7-36, -37 또는 38)-E, ($Lys^{26,34}$-비스(N_ε-알카노일))hGLP-1(7-36, -37 및 -38)-E, (Arg^{26}, Lys^{34}(N_ε-알카노일))hGLP-1(8-36, -37 또는 -38)-E, ($Arg^{26,34}$, Lys^{36}(N_ε-알카노일)) hGLP-1(7-36, -37 또는 -38)-E 또는 ($Arg^{26,34}$, Lys^{38}(N_ε-알카노일))hGLP-1 (7-38)-E—여기서 E는 -OH 및 $-NH_2$임—가 아니고;

(iv) 화학식(Ⅰ)의 화합물은 Z^1-hGLP-1(7-36, -37 또는 -38)-OH, Z^1-hGLP-1(7-36, -37 또는 -38)-NH_2가 아니며, 이때 Z^1은 다음으로 이루어지는 군으로부터 선택되고:

(a) (Arg^{26}), (Arg^{34}), ($Arg^{26,34}$), (Lys^{36}), (Arg^{26}, Lys^{36}), (Arg^{34}, Lys^{36}), (D-Lys^{36}), (Arg^{36}), (D-Arg^{36}), ($Arg^{26,34}$, Lys^{36}) 또는 ($Arg^{26,36}$, Lys^{34});

(b) (Asp^{21});

(c) (Aib^{8}), (D-Ala^{8}) 및 (Asp^{9}) 중 적어도 하나; 및

(d) (Tyr^{7}), (N-아실-His^{7}), (N-알킬-His^{7}), (N-아실-D-His^{7}) 및 (N-알킬-D-His^{7});

(v) 화학식(Ⅰ)의 화합물은 (a) 내지 (d) 군에 기재된 임의의 두 치환기의 조합체가 아니고;

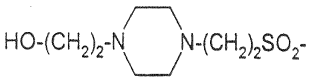
(vi) 화학식(Ⅰ)의 화합물은 (N-Me-Ala^{8})hGLP-1(8-36 또는 -37), (Glu^{15}) hGLP-1(7-36 또는 -37), (Asp^{21})hGLP-1(7-36 및 -37) 및 (Phe^{31})hGLP-1(7-36 및 -37)이다.

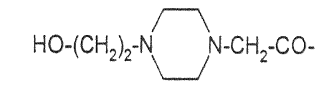
상기 화합물들 중 바람직한 군의 화합물은 A^{11}은 Thr이고; A^{13}은 Thr이고; A^{15}는 Asp이고; A^{17}은 Ser이고; A^{18}은 Ser 또는 Lys이고; A^{21}은 Glu이고; A^{23}은 Gln 또는 Glu이고; A^{27}은 Glu, Leu, Aib 및 Lys로 이루어지는 군으로부터 선택되고; A^{31}은 Trp, Phe 및 β-Nal로 이루어지는 군으로부터 선택되는 화합물; 또는 제약학적으로 허용 가능한 이들의 염이다.

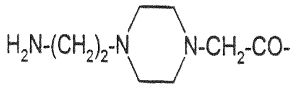
상기 화합물들 중 바람직한 군의 화합물은 A^{9}는 Glu, N-Me-Glu 및 N-Me-Asp로 이루어지는 군으로부터 선택되고; A^{12}는 Phe, Acc, β-Nal 및 Aic로 이루어지는 군으로부터 선택되고; A^{16}은 Val, Acc 및 Aib로 이루어지는 군으로부터 선택되고; A^{19}는 Tyr 또는 β-Nal이고; A^{20}은 Leu, Acc 및 Cha로 이루어지는 군으로부터 선택되고; A^{24}는 Ala, Aib 및 Acc로 이루어지는 군으로부터 선택되고; A^{25}는 Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 및 HN-CH($(CH_2)_e$-X^3)-C(O)로 이루어지는 군으로부터 선택되고; A^{28}은 Phe 또는 β-Nal이고; A^{29}는 Ile 또는 Acc이고; A^{30}은 Ala 또는 Aib이고; A^{32}는 Leu, Acc 및 Cha로 이루어지는 군으로부터 선택되고; A^{33}은 Val, Lys 및 Acc로 이루어지는 군으로부터 선택되는 화합물; 또는 제약학적으로 허용 가능한 이들의 염이다.

상기 화합물들 중 바람직한 군의 화합물은 A^{8}은 Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala 및 N-Me-Gly로 이루어지는 군으로부터 선택되고; A^{10}은 Gly이고; A^{12}는 Phe, β-Nal, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{16}은 Val, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{20}은 Leu, A6c, A5c 및 Cha로 이루어지는 군으로부터 선택되고; A^{22}는 Gly, β-Ala 및 Aib로 이루어지는 군으로부터 선택되고; A^{24}는 Ala 또는 Aib이고; A^{29}는 Ile, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{32}는 Leu, A6c, A5c 및 Cha로 이루어지는 군으로부터 선택되고; A^{33}은 Val, Lys, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{35}는 Aib, β-Ala, Ado, A6c, A5c, D-Arg 및 Gly로 이루어지는 군으로부터 선택되고; A^{37}은 Gly, Aib, β-Ala, Ado, D-Ala, Ava, Asp, Aun, D-Asp, D-Arg, Aec 및 HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O)로 이루어지는 군으로부터 선택되나 결실인 화합물; 또는 제약학적으로 허용 가능한 이들의 염이다.

상기 화합물들 중 바람직한 군의 화합물은 각각의 경우에 대하여 X^4는 -C(O)-이고; R^1은 OH 또는 NH_2인 화합물; 또는 제약학적으로 허용 가능한 이들의 염이다.

상기 화합물들 또는 제약학적으로 허용 가능한 이들의 염의 바람직한 화합물군은 R^2는 H이고 R^3은 (C_1-C_{30})알킬, (C_2-C_{30})알케닐, (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, 

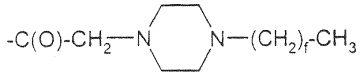
, 

또는 

인 것들이다.

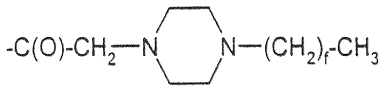
화학식(Ⅰ)을 가지는 바람직한 화합물은 A^{8}은 Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala 및 N-Me-Gly로 이루어지는 군으로부터 선택되고; A^{10}은 Gly이고; A^{12}는 Phe, β-Nal, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{16}은 Val, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{20}은 Leu, A6c, A5c 및 Cha로 이루어지는 군으로부터 선택되고; A^{22}는 Gly, β-Ala 및 Aib로 이루어지는 군으로부터 선택되고; A^{24}는 Ala 또는 Aib이고; A^{29}는 Ile, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{32}는 Leu, A6c, A5c 및 Cha로 이루어지는 군으로부터 선택되고; A^{33}은 Val, Lys, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{35}는 Aib, β-Ala, Ado, A6c, A5c, D-Arg 및 Gly로 이루어지는 군으로부터 선택되고; A^{37}은 Gly, Aib, β-Ala, Ado, D-Ala, Ava, Asp, Aun, D-Asp, D-Arg, Aec 및 HN-CH($(CH_2)_n$-

$N(R^{10}R^{11}))$-C(O)로 이루어지는 군으로부터 선택되나 결실이고; 각각의 경우에 대하여 X^4는 -C(O)-이고; e는 각각의 경우에 대하여 독립적으로 1 또는 2이고; R^1은 OH 또는 NH_2이며; R^{10}은 (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐 또는



이고, R^{11}은 H인 화합물; 또는 제약학적으로 허용 가능한 이들의 염이다.

상기 화합물들 중 보다 바람직한 화합물은 R^{10}이 (C_4-C_{20})아실, (C_4-C_{20})알킬술포닐 및



로 이루어지는 군으로부터 선택되는 화합물; 또는 제약학적으로 허용 가능한 이들의 염이다.

화학식(Ⅰ)을 가지는 보다 바람직한 화합물은 다음과 같은 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염이다:

$(Aib^{8,35})hGLP-1(7-36)NH_2$,

$((N_\alpha-HEPES-HiS)^7, Aib^{8,35})hGLP-1(7-36)NH_2$,

$((N_\alpha-HEPA-HiS)^7, Aib^{8,35})hGLP-1(7-36)NH_2$,

$(Aib^8, \beta-Ala^{35})hGLP-1(7-36)NH_2$,

$*(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_\varepsilon-$테트라데카노일$)hGLP-1(7-36)NH_2$,

$(Aib^{8,35}, Ala^{26}, Lys^{34}(N_\varepsilon-$테트라데카노일$)hGLP-1(7-36)NH_2$,

$(Aib^{8,35,37}, Ala^{26,34}, Lys^{38}(N_\varepsilon-$테트라데카노일$)hGLP-1(7-38)NH_2$,

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_\varepsilon-$데카노일$)hGLP-1(7-36)NH_2$,

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_\varepsilon-$도데칸술포닐$)hGLP-1(7-36)NH_2$,

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_\varepsilon-$(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 $(7-36)NH_2$,

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}$(1-(4-테트라데실-피페라진)))$hGLP-1(7-36)NH_2$,

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}$(1-테트라데실아미노))$hGLP-1(7-36)NH_2$,

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_\varepsilon-$테트라데카노일$), \beta-Ala^{37})hGLP-1(7-37)-OH$, 또는

$(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_\varepsilon-$테트라데카노일$))hGLP-1(7-36)-OH$.

상기 군의 화합물들 중 보다 바람직한 화합물은 다음과 같은 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염이다:

$(Aib^{8,35})hGLP-1(7-36)NH_2$,

$(Aib^8, \beta-Ala^{35})hGLP-1(7-36)NH_2$,

$(Aib^{8,35}, Arg^{26}, Lys^{34}(N_\varepsilon-$테트라데카노일$)hGLP-1(7-36)NH_2$,

$(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_\varepsilon-$테트라데카노일$)hGLP-1(7-38)NH_2$,

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일)hGLP-1(7-36)NH_2, 또는

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일), β-Ala^{37})hGLP-1(7-37)-OH.

화학식(Ⅰ)을 가지는 보다 바람직한 그 밖의 다른 화합물은 다음과 같은 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염이다:

(Aib^{8,35}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23})hGLP-1(7-36)NH_2;

(Aib^{8,24,35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-Aec-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2;

(Aib^{8,35}, Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2;

(Aib^{8,17,35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH_2;

(Gly^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Ser^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{22,33}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Leu^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{33}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, Leu^{27},β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH_2;

(Aib^{8}, Lys^{18,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Phe^{31}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N_ε-데카노일)hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-데카노일)hGLP-1(7-36)NH_2;

*(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-도데카노일)hGLP-1(7-36)NH_2;

(Aib^{8}, B-Ala^{35}, Ser^{37}(O-데카노일)hGLP-1(7-37)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38}, Lys^{39}(N_ε-옥타노일)hGLP-1(7-39)NH_2;

(Aib[8], Arg[26,34], β-Ala[35], Lys[37](N_ε-옥타노일)hGLP-1(7-37)NH_2;

(Aib[8], Arg[26,34], β-Ala[35], Lys[37](N_ε-데카노일)hGLP-1(7-37)NH_2; 또는

(Aib[8], Arg[26,34], β-Ala[35], Lys[37](N_ε-테트라데카노일)hGLP-1(7-37)NH_2.

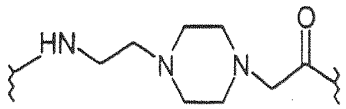
화학식(1)을 가지는 보다 바람직한 다른 화합물은 이하의 본 발명의 실시예들에서 특정하게 제시되는 각각의 화합물 또는 제약학적으로 허용 가능한 이들의 염이다.

다른 양태에서, 본 발명은 상기에서 한정된 바와 같은 화학식(Ⅰ)을 가지는 유효량의 화합물 또는 제약학적으로 허용 가능한 이들의 염 및 제약학적으로 허용 가능한 담체 또는 부형제를 포함하는 약제 조성물을 제공한다.

다른 양태에서, 본 발명은 필요로 하는 대상 내에서 GLP-1 수용체로부터 아고니스트 작용(agonist effect)를 유도하는 방법을 제공하며, 상기 방법은 상기에서 한정된 바와 같은 화학식(Ⅰ)을 가지는 유효량의 화합물 또는 제약학적으로 허용 가능한 이들의 염을 상기 대상에 투여하는 단계를 포함한다.

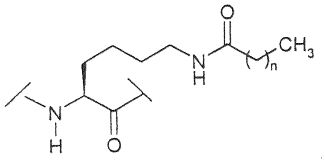
또 다른 양태에서, 본 발명은 필요로 하는 환자 내에서 I형 당뇨병, II형 당뇨병, 비만증, 글루카곤종, 기도의 분비 장애, 대사 장애, 관절염, 골다공증, 중추신경계 질환, 협착증, 신경변성 질환, 신부전, 충혈성 심부전, 신증, 경화, 폐수종, 고혈압, 및 음식물 섭취에 있어 감소가 요구되는 질환으로 이루어지는 군으로부터 선택되는 질환을 치료하는 방법이 제공되며, 상기 방법은 상기에서 한정된 화학식(Ⅰ)을 가지는 유효량의 화합물 또는 제약학적으로 허용 가능한 이들의 염을 상기 대상에 투여하는 단계를 포함한다. 상기 방법은 치료되는 질환이 I형 당뇨병 또는 II형 당뇨병인 경우에 보다 바람직하다.

N-말단 아미노산을 제외하고, 본 명세서에 기재된 모든 아미노들의 약어(예를 들면, Ala)는 -NH-CH(R)-CO-의 구조식을 의미하는 것으로서, 이때 R은 아미노산의 측쇄(예를 들면, Ala의 경우에는 CH_3)이다. N-말단 아미노산에 대한 약어는 (R^2R^3)-N-CH(R)-CO-의 구조식을 의미하며, 여기서 R은 아미노산의 측쇄이고, R^2 및 R^3은 A^7이 Ura, Paa 또는 Pta인 경우를 제외하고는 상기에서 한정된 바와 같고, 본 명세서에서 Ura, Paa 또는 Pta는 아미노기가 제거된 아미노산으로 간주되기 때문에, A^7이 Ura, Paa 또는 Pta인 경우에 R^2 및 R^3은 존재하지 않는다. Amp, β-Nal, Nle, Cha, 3-Pal, 4-Pal 및 Aib는 각각 4-아미노-페닐알라닌, β-(2-나프틸)알라닌, 노르류신, 사이클로헥실알라닌, β-(3-피리디닐)알라닌, β-(4-피리디닐)알라닌 및 α-아미노이소부티르산과 같은 α-아미노산의 약어들이다. 그 밖의 아미노산들은 다음과 같이 지정된다: Ura는 우로칸산이고; Pta는 (4-피리딜티오) 아세트산이고; Paa는 트랜스-3-(3-피리elf) 아클릴산이고; Tma-His는 N,N-테트라메틸아미노-히스티딘이고; N-Me-Ala는 N-메틸-알라닌이고; N-Me-Gly는 N-메틸-글리신이고; N-Me-Glu는 N-메틸-글루탐산이고; Tle는 tert-부틸글리신이고; Abu는 α-아미노부티르산이고; Tba는 tert-부틸알라닌이고; Orn은 오르니틴이고; Aib는 α-아미노이소부티르산이고; β-Ala는 β-알라닌이고; Gaba는 ɣ-아미노부티르산이고; Ava는 5-아미노발레르산이고; Ado는 12-아미노도데카노산이고; Aic는 2-아미노인단-2-카르복시산이고; Aun은 11-아미노운데카노산이며; Aec는 다음과 같은 구조식을 가지는 4-(2-아미노에틸)-1-카르복시메틸-피페라진이다:

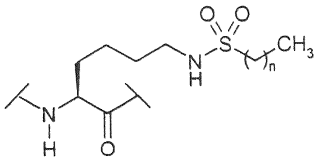


Acc는 1-아미노-1-사이클로프로판카르복시산(A3c); 1-아미노-1-사이클로부탄카르복시산(A4c); 1-아미노-1-사이클로펜탄카르복시산(A5c); 1-아미노-1-사이클로헥산카르복시산(A6c); 1-아미노-1-사이클로헵탄카르복시산(A7c); 1-아미노-1-사이클로옥탄카르복시산(A8c); 및 1-아미노-1-사이클로노난카르복시산(A9c)으로 이루어지는 군으로부터 선택되는 아미노산을 의미한다. 상기 식에서, 하이드록시알킬, 하이드록시페닐알킬 및 하이드록시나프틸알킬은 1,4-하이드록시 치환기를 함유할 수 있다. COX[5]는 -C=·X[5]를 나타낸다. -C=·X[5]의 예로는 아세틸 및 페닐프로피오닐을 들 수 있으나, 이들로 제한되는 것은 아니다.

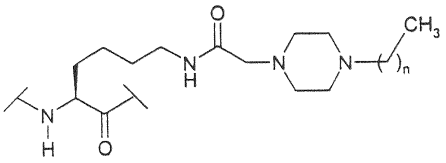
Lys(N_ε-알카노일)은 하기 구조식으로 나타내진다:



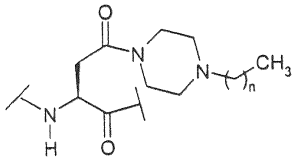
Lys(N_ε-알킬술포닐)은 하기 구조식으로 나타내진다:



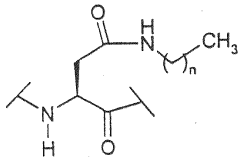
Lys(N_{ε}-(2-(4-알킬-1-피페라진)-아세틸)은 하기 구조식으로 나타내진다:



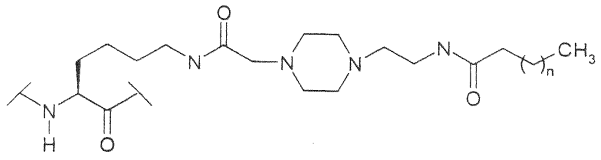
Asp(1-(4-알킬-1-피페라진)은 하기 구조식으로 나타내진다:



Asp(1-(4-알킬아미노)는 하기 구조식으로 나타내진다:

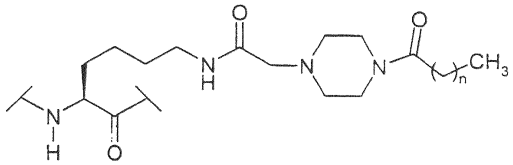


Lys(N_{ε}-Aec-알카노일)은 하기 구조식으로 나타내진다:



상기 구조식들에서 변수 n은 1부터 30에 속하는 정수 중 하나이다.

Lys(N_{ε}-Ace-알카노일)은 하기 구조식으로 나타내진다:



본 명세서에서 사용되는 그 밖의 약어들의 완전한 명칭은 다음과 같다: Boc는 t-부틸옥시카보닐을 의미하고, HF는 플루오르화수소를 의미하고, Fm은 포르밀을 의미하고, Xan은 크산틸을 의미하고, Bzl은 벤질을 의미하고, Tos는 토실을 의미하고, DNP는 2,4-디니트로페닐을 의미하고, DMF는 디메틸포름아미드를 의미하고, DCM은 디클로로메탄을 의미하고, HBTU는 2-(1H-벤조트리아졸-1-일)-1,1,3,3-테트라메틸 우로늄 헥사플루오로포스페이트를 의미하고, DIEA는 디이소프로필에틸아민을 의미하고, HOAc는 아세트산을 의미하고, TFA는 트리플루오로아세트산을 의미하고, 2ClZ는 2-클로로벤질옥시카보닐을 의미하고, 2BrZ는 2-브로모벤질옥시카보닐을 의미하고, OcHex는 O-사이클로헥실을 의미하고, Fmoc는 9-플루오레닐메톡시카보닐을 의미하고, HOBt는 N-하이드록시벤조트리아졸을 의미하며, PAM 수지는 4-하이드록시메틸페닐아세트아미도메틸 수지를 의미한다.

"할로"란 용어는 플로오로, 클로로, 브로모 및 요오드를 포함한다.

"(C_1-C_{30})탄화수소 모이어티란 용어는 알킬, 아케닐 및 알키닐을 포함하며, 알케닐 및 알키닐의 경우에는 C_2-C_{30}이다.

또한, 본 발명의 펩타이드는 본 명세서에서, 예를 들면 (A5c^8)hGLP-1(7-36)NH_2와 같이 처음 한 쌍의 괄호 안에 천연 서열로부터 유래되는 치환 아미노산(예를 들면, A5c^{8}은 hGLP-1 내의 Ala^{8}을 의미함)을 가지는 다른 형식으로 나타내진다. 약어인 GLP-1은 글루카곤형 펩타이드-1을 의미하고; hGLP-1은 인간의 글루카곤형 펩타이드-1을 의미한다. 괄호 안의 수들는 펩타이드 내에 존재하는 아미노산의 수를 의미한다(예를 들면, hGLP-1(7-36)은 인간의 GLP-1에 대한 펩타이드 서열의 7번 아미노산부터 36번 아미노산이다). hGLP-1(7-37)에 대한 서열은 Mojsov, S의 Int. J. Peptide Protein Res., 40, 1992, pp. 333-342에 기재되어 있다. hGLP-1(7-36)NH_2에서 "NH_2"는 펩타이드의 C-말단이 아미드화되었음을 가리킨다. hGLP-1(7-36)은 C-말단이 유리산임을 의미한다. hGLP-1(7-38)에서 37번 및 38번 위치의 잔기는 각각 Gly 및 Arg이다.

본 발명의 펩타이드는 표준 고체상 펩타이드 합성에 의해 제조될 수 있으며, 이러한 합성방법은 예를 들면 Stewart, J.M 등의 Solid Phase Synthesis(Pierce Chemical Co., 2d ed, 1984)를 참조한다. 상기 일반식의 R^2 및 R^3 치환기는 당 기술분야에 공지된 표준 방법에 의하여 N-말단 아미노산의 유리 아민기에 부착될 수 있다. 예를 들면, (C_1-C_{30})알킬과 같은 알킬기는 환원성 알킬화를 사용하여 부착될 수 있고, (C_1-C_{30})하이드록시알킬과 같은 하이드록시알킬기 또한 환원성 알킬화를 사용하여 부착될 수 있으며, 이때 유리 하이드록시기는 t-부틸 에스테르에 의해 보호된다. 예를 들면, COE^{1}과 같은 아실기는 기성 수지를 메틸렌 클로라이드 내의 3몰 당량의 유리산 및 디이소프로필카보디이미드와 1시간 동안 혼합하여 예를 들면 E^{1}COOH와 같은 유리산을 N-말단 아미노산의 유리 아민기에 커플링함으로써 부착될 수 있다. 유리산이 유리 하이드록시기, 예를 들면 p-하이드록시페닐프로피온산을 함유하는 경우에는 3몰 당량의 부가적인 HOBT를 함께 사용하여 커플링을 수행해야 한다.

R^1이 NH-X^2-CH_2-$CONH_2$인 경우(즉, Z^0=$CONH_2$인 경우), MBHA 수지에 커플링된 BocHN-X^2-CH_2-COOH를 사용하여 펩타이드 합성을 시작한다. R^1이 NH-X^2-CH_2-COOH인 경우(즉, Z^0 = COOH)에는 PAM 수지에 커플링된 Boc-HN-X^2-CH_2-COOH를 사용하여 펩타이드 합성이 시작된다. 이러한 특정한 단계에는 4몰 당량의 Boc-HN-X^2-CH_2-COOH, HBTU 및 HOBt와 10몰 당량의 DIEA가 사용된다. 커플링에 소요되는 시간은 약 8시간이다.

보호된 아미노산인 1-(N-tert-부톡시카보닐-아미노)-1-사이클로헥산-카르복시산(Boc-A6c-OH)를 다음과 같이 합성하였다. 19.1 g(0.133 몰)의 1-아미노-1-사이클로헥산카르복시산(Acros Organics, Fisher Scientific, Pittsburgh, PA)를 200 ㎖의 디옥산과 100 ㎖의 물에 용해시키고, 여기에 67 ㎖의 2N NaOH를 첨가하였다. 용액을 얼음물 중탕으로 냉각하고, 32.0 g(0.147 몰)의 디-tert-부틸-디카보네이트를 상기 용액에 첨가하였다. 반응 혼합물을 실온에서 하룻밤 동안 교반한 뒤, 감압 하에서 다이옥산을 제거하고, 남은 수용액에 200 ㎖의 에틸 아세테이트를 첨가하였다. 혼합물을 얼음물 중탕으로 냉각하고, 4N HCl을 첨가하여 수층의 pH를 약 3으로 조절한 뒤, 유기층을 분리하였다. 에틸 아세테이트(1×100 ㎖)를 사용하여 수층을 추출하였다. 두 유기층을 섞고 물(2×150 ㎖)로 세척한 뒤, 무수 $MgSO_4$ 상에서 건조하고, 여과한 다음, 감압 하에서 건조한 상태가 되도록 농축하였다. 잔류물을 에틸 아세테이트/헥산 내에서 재결정화하여, 9.2 g의 순수한 산물을 얻었으며, 이때 수율은 29%이었다.

Boc-A6c-OH의 합성 방식과 유사한 방식으로 Boc-A5c-OH를 합성하였다. 당업자들은 본 발명의 방법과 유사한 방식으로 보호된 다른 Acc 아미노산을 제조할 수 있을 것이다.

A5c, A6c 및/또는 Aib를 함유하는 본 발명의 GLP-1 유사체의 합성 시, 이들 잔기 및 그 바로 뒤에 오는 잔기의 커플링에 소요되는 시간은 2시간이다. (Tma-His^7)hGLP-1(7-36)NH_2의 합성 시, 마지막 커플링 반응에서 펩타이드-수지의 N-말단 유리 아민과의 반응에는 4 ㎖ DMF 내의 HBTU(2 mmol)과 DIEA(0.1 ㎖)가 사용되고, 커플링에 소요되는 시간은 약 2시간이다.

상기 일반식의 R^2 및 R^3 치환기는 당 기술분야에 공지된 표준 방법에 의해 N-말단 아미노산의 유리 아민에 부착될 수 있다. 예를 들면 (C_1-C_{30})알킬과 같은 알킬기들은 환원성 알킬화를 사용하여 부착될 수 있으며, 예를 들면 (C_1-C_{30})하이드록시알킬과 같은 하이드록시알킬기 또한 환원성 알킬화를 사용하여 부착될 수 있고, 이때 유리 하이드록시기는 t-부틸 에스테르에 의해 보호된다. 예를 들면 COX^{1}와 같은 아실기는 기성 수지를 메틸렌 클로라이드 내의 3몰 당량의 유리산 및 디이소프로필카보디이미드와 1시간 동안 혼합하여, 예를 들면 X^{1}COOH와 같은 유리산을 N-말단 아미노산에 커플링함으로써 부착될 수 있다. 유리산이 유리 하이드록시기, 예를 들면 p-하이드록시페닐프로피온산을 함유하는 경우에는 3몰 당량의 부가의 HOBT를 사용하여 커플링을 수행해야 한다.

다음과 같은 절차에 따라 본 발명의 화합물에 대하여 GLP-1 결합 화합물로서의 활성을 테스트하였다.

세포 배양:

5% CO_2/95% 공기로 이루어지는 습한 대기 중에서 10%의 송아지 태아 혈청을 함유하는 약 37℃로 유지된 Dulbeco's modified Eagle's medium(DMEM) 내에서 GLP-1 수용체를 발현하는 RIN 5F 래트의 인슐린종 세포(ATCC-# CRL-2058, American type Culture Collection, Manassas, VA)를 배양하였다.

방사성 리간드 결합:

Brinkman Polytron(Westbury, NY)을 함유하는 20 ㎖의 차가운 50 mM 트리스-HCl 내에서 RIN 세포들을 균질화하여(6, 15초로 세팅) 방사성 리간드 결합 분석을 위한 막을 준비하였다. 균질화물을 원심분리(39,000 g, 10분)하여 2회 세척하고, 2.5mM $MgCl_2$, 0.1 mg/㎖의 바시트라신(Sigma Chemical, St. Louis, MO) 및 0.1%의 BSA를 함유하는 50mM 트리스-HCl 내에서 최종 펠릿을 재현탁하였다. 함량 분석을 위하여, 0.05nM (^{125}I)GLP-1(7-36)(~2200 Ci/mmol, New England Nuclear, Boston, MA)을 사용하고, 0.05 ㎖의 경쟁 테스트용 비표지 펩타이드를 사용한 것과 사용하지 않은 조건에서 분액(0.4 ㎖)을 배양하였다. 100분 동안 배양한 후(25℃), 0.5%의 폴리에틸렌이민에 사전 침지되었던 GF/C 필터(Brandel, Gaithersburg, MD)를 통해 급속 여과하여 결합된 (^{125}I)GLP-1(7-36)과 유리된 (^{125}I)GLP-1(7-36)을 분리하였다. 그런 다음, 5 ㎖의 차가운 50mM 트리스-HCl 분액을 사용하여 필터를 3회 세척하고, 감마 분광기(Wallac LKB, Gaithersburg, MD)를 사용하여 필터 상에 포획된 결합 방사능을 계측하였다. 결합된 총 (^{125}I)GLP-1(7-36)에서 100nM (^{125}I)GLP-1(7-36)(Bachem, Torrence, CA)의 존재 하에서 결합된 것들을 뺀 값을 고유 결합(Specific binding)으로 정의 하였다.

본 발명의 펩타이드는 제약학적으로 허용 가능한 염의 형태로 제공될 수 있다. 이러한 염의 예로는 유기산들(예를 들면, 아세트산, 락트산, 말레산, 시트르산, 말산, 아스코르브산, 숙신산, 벤조산, 메탄설폰산, 톨루엔설폰산 또는 파모산), 무기산들(예를 들면, 염산, 황산 또는 인산) 및 폴리머산들(예를 들면, 탄산(tannic acid), 카르복시메틸 셀룰로오스, 폴리락트산, 폴리글리콜산 또는 폴리락트산-글리콜산의 코폴리머)로 형성된 것들이 있으나, 이들로 제한되는 것은 아니다. 본 발명의 펩타이드 염을 제조하는 대표적인 방법은 당 기술분야에 공지된 것으로서, 표준 염 교환법에 의해 수행될 수 있다. 따라서, 본 발명의 펩타이드의 TFA 염(TFA 염은 제조용 HPLC를 사용하여 상기 펩타이드를 정제하고, TFA 함유 완충 용액을 용리시킴으로써 얻어짐)은 소량의 0.25N 아세트산 수용액 내에 상기 펩타이드를 용해시킴으로써 아세테이트 염과 같은 다른 염으로 전환될 수 있다. 얻어지는 용액을 반제조용(semi-prep) HPLC 칼럼(Zorbax, 300 SB, C-8)에 건다. 칼럼은 (1) 0.1N 암모늄 아세테이트 수용액으로 0.5시간 동안, (2) 0.25N 아세트산 수용액으로 0.5시간 동안, 및 (3) 4 ㎖/분 유속의 직선 구배(20%에서 100%의 B 용액, 30분)로 칼럼을 용리시킨다(A 용액은 0.25N 아세트산 수용액이고; B 용액은 아세토니트릴/물(80:20) 내의 0.25N 아세트산이다). 펩타이드를 함유하는 분획들을 수집하여 동결 건조한다.

당업자들에게 공지된 바와 같이, GLP-1의 공지된 용도 및 잠재적 용도는 다양하고 광대하다(Todd, J.F. 등의 Clinical Science, 1998, 95, pp. 325-329; 및 Todd J.F. 등의 European Journal of Clinical Investigation, 1997, 27, pp. 533-536 참조). 따라서, 아고니스트 작용를 유도하기 위하여 본 발명의 화합물을 투여하는 것도 GLP-1 자체와 동일한 효과 및 용도를 가질 수 있다. GLP-1은 I형 당뇨병, II형 당뇨병, 비만증, 글루카곤종, 기도의 분비 장애, 대사 장애, 관절염, 골다공증, 중추신경계 질환, 협착증, 신경변성 질환, 신부전, 충혈성 심부전, 신증, 경화, 폐수종, 고혈압, 및 음식물 섭취에 있어 감소가 요구되는 질환의 치료에 다양하게 사용될 수 있다. 대상으로부터 아고니스트 작용를 유도하는 본 발명의 GLP-1 유사체는 위장 절제 또는 소장 절제와 관련된 저혈당 및 흡수 불량증의 치료에 사용될 수 있다.

따라서, 본 발명은 본 발명의 범위 내에서 활성 성분으로서 화학식(Ⅰ)을 가지는 적어도 하나의 화합물과 제약학적으로 허용 가능한 담체를 포함하는 약제 조성물을 포함한다.

본 발명의 조성물 내의 활성 성분의 투약량은 다양할 수 있으나, 활성 성분의 양은 적절한 투약 형태가 얻어지는 정도의 양이어야 한다. 선택된 투약량은 원하는 치료 효과, 투여 경로 및 치료 기간에 따라 결정된다. 일반적으로, 본 발명의 활성제에 대한 유효 투약량은 1×10^{-7} 내지 200 mg/kg/일이고, 바람직하게는 1×10^{-4} 내지 100 mg/kg/일이며, 이는 1회 분량으로 투여되거나 다수 분량으로 나누어 투여될 수 있다.

본 발명의 화합물은 경구, 비경구(예를 들면, 근육내, 복막내, 정맥내, 또는 피하내 주사 또는 삽입), 비강, 질, 직장, 설하, 또는 국부적인 투여경로를 통해 투여될 수 있으며, 각각의 투여경로에 적합한 투약형태를 제공하는 제약학적으로 허용 가능한 담체와 함께 제형화될 수 있다.

경구 투여를 위한 고형 투약 형태로는 캡슐, 정제, 환약, 분말, 및 과립이 있다. 이러한 고형 투약형태에서, 활성성분은 수크로스, 락토스, 또는 전분과 같은 제약학적으로 허용 가능한 적어도 하나의 불활성 담체와 혼합된다. 또한, 이러한 투약 형태는 정상적으로는 이러한 불활성 희석제 이외의 부가의 물질, 예를 들면 마그네슘 스테아레이트와 같은 윤활제를 포함할 수 있다. 캡슐, 정제, 및 환약의 경우에도 투약 형태에 완충제가 포함될 수 있다. 정제 및 환약은 부가적으로 장코팅(enteric coating)을 가지는 형태로 제조될 수 있다.

경구 투여를 위한 액상 투약 형태는 제약학적으로 허용 가능한 에멀젼, 용액, 현탁액, 시럽, 및 물과 같이 당 기술분야에서 통상적으로 사용되는 불활성 희석제를 함유하는 일릭서(elixir)를 포함한다. 조성물은 또한 이러한 불활성 희석제 외에도 습윤제, 에멀젼화제, 및 현탁제와 같은 보조제(adjuvant), 및 감미료, 향미료, 및 향료를 포함할 수 있다.

본 발명에 따르는 비경구 투여용 제제는 멸균 수용액 또는 비수계 용액, 현택액, 또는 에멀젼을 포함한다. 비수계 용매 또는 부형제의 예로는 프로필렌 글리콜, 폴리에틸렌 글리콜, 올리브유 및 옥수수 기름와 같은 식물성 기름, 젤라틴, 및 에틸 올리에이트와 같은 주사 가능한 유기 에스테르가 있다. 이러한 투약형태 또한 보존제, 습윤제, 에멀젼화제, 및 분산제와 같은 보조제를 함유할 수 있다. 예를 들면, 박테리아-차단 필터를 통한 여과, 조성물 내로의 멸균제 첨가, 조성물로의 방사선 조사, 또는 조성물의 가열을 통하여 이들을 살균할 수 있다. 또한, 이러한 제제는 멸균수에 용해될 수 있는 멸균된 고형 조성물 또는 기타 주사 가능한 멸균 매질의 형태로 사용 직전에 제조될 수 있다.

직장 또는 질 투여용 조성물은 활성성분 외에도 코카 버터 또는 좌약 왁스와 같은 부형제를 함유할 수 있는 좌약이 바람직하다.

비강 또는 설하 투여용 조성물 또한 당 기술분야에 공지된 표준 부형제를 함유하는 상태로 제조된다.

본 발명의 조성물은 하기 특허들 및 특허 출원에 기재된 것과 같은 서방형(sustained release) 조성물의 형태로 투여될 수 있다. 미국특허 제5,672,659호에는 생활성제 및 폴리에스테르를 포함하는 서방형 조성물이 제시되어 있다. 미국특허 제5,595,760호에는 겔화 가능한 형태의 생활성제를 포함하는 서방형 조성물이 제시되어 있다. 1997년 9월 9일에 출원된 미국출원 제08/929,363호에는 생활성제 및 키토산을 포함하는 서방형 조성물이 제시되어 있다. 1996년 11월 1일에 출원된 미국출원 제08/740,778호에는 생활성제 및 사이클로덱스트린을 포함하는 서방형 조성물이 제시되어 있다. 1998년 1월 29일에 출원된 미국출원 제09/015,394호에는 생활성제의 흡수성 서방형 조성물이 제시되어 있다. 1998년 7월 23일에 출원된 미국출원 제09/121,653호에는 수중 유적형(oil-in-water) 공정으로 펩타이드와 같은 치료제를 포함하는 마이크로입자를 제조하는 방법이 제시되어 있다. 1998년 8월 10일에 출원된 미국출원 제09/131,472호에는 펩타이드 및 포스포릴화 폴리머와 같은 치료제를 포함하는 복합체가 제시되어 있다. 1998년 11월 2일에 출원된 미국출원 제098/184,413호에는 비중합성 락톤을 함유하는 펩타이드 및 폴리머와 같은 치료제를 포함하는 복합체가 제시되어 있다. 상기 특허들 및 출원들의 내용은 본 발명에 참고로 인용되었다.

특별히 한정하지 않는 한, 본 명세서에 사용된 모든 기술 용어 및 과학 용어는 당업자들이 보편적으로 이해하는 의미와 동일한 의미를 갖는다. 또한, 본 명세서에 참고로 인용된 모든 공보, 특허출원, 특허 및 기타 문헌은 참고로 인용되었다.

하기 실시예들은 본 발명의 펩타이드를 제조하기 위한 합성 방법들을 설명한 것으로서, 이들 방법은 당 기술분야에 공지되어 있다. 당 기술분야에는 그 밖의 다른 방법들도 알려져 있다. 하기 실시예는 본 발명을 설명하기 위한 것이며, 이들 실시예는 어떠한 방식으로든 본 발명을 제한하지 않는다.

Boc-βAla-OH, Boc-D-Arg(Tos)-OH 및 Boc-D-Asp(OcHex)는 Nova Biochem(San Diego, Califonia)사로부터 구입하였다. Boc-Aun-OH는 Bachem사(King of Prussia, PA)로부터 구입하였다. Boc-Ava-OH 및 Boc-Ado-OH는 Chem-Impex International사(Wood Dale, IL)로부터 구입하였다. Boc-Nal-OH는 Synthech, Inc사(Albany, OR)로부터 구입하였다.

[실시예]

실시예 1

$(Aib^{8,35})hGLP-1(7-36)NH_2$

Boc-화학성 고체상 펩타이드 합성을 가속화하도록 변형된 Applied Biosystems사(Foster City, CA)의 모델 430A 펩타이드 합성기 상에서 표제 화합물을 합성하였다. Schnolzer 등의 Int. J. Peptide Protein Res., 90:180(1992)을 참조한다. 0.91 mmol/g의 치환율을 가지는 4-메틸벤질하이드릴아민(MBHA) 수지(Peninsula, Beltmont, CA)가 사용되었다. Boc 아미노산으로는 Boc-Ala-OH, Boc-D-Arg(Tos)-OH, Boc-Asp(OcHex)-OH, Boc-Tyr(2BrZ)-OH, Boc-His(DNP)-OH, Boc-Val-OH, Boc-Leu-OH, Boc-Gly-OH, Boc-Gln-OH, Boc-Ile-OH, Boc-Lys(2ClZ)-OH, Boc-Thr(Bzl)-OH, Boc-Ser(Bzl)-OH, Boc-Phe-OH, Boc-Aib-OH, Boc-Glu(OcHex)-OH 및 Boc-Trp(Fm)-OH와 같은 측쇄 보호기를 가지는 아미노산(Bachem, CA, Torrance, CA; Nova Biochem., LaJolla, CA)이 사용되었다. 합성은 0.20 mmol 규모로 수행되었다. 2×1분 동안 100% TFA로 처리하여 Boc기를 제거하였다. 4㎖의 DMF 내의 HBTU(2.0 MMOL) 및 DIEA(1.0 ㎖)를 사용하여 Boc 아미노산(2.5 mmol)을 사전 활성화하고, 펩타이드 수지 TFA 염의 사전 중화 없이 커플링하였다. Boc-Aib-OH 잔기 및 다음 잔기인 Boc-Lys(2ClZ)-OH 및 Boc-His(DNP)-OH의 커플링에 소요된 시간은 2시간이었고, 이들을 제외한 나머지 잔기들에 대한 커플링 시간은 5분이었다.

펩타이드 사슬 조립의 마지막 단계에서, 2×30분 동안 DMF 내의 20% 머켑토에탄올/10% DIEA 용액으로 잔기를 처리하여, His 측쇄 상의 DNP기를 제거하였다. 그런 다음, 100% TFA로 2×2분 동안 처리하여 N-말단의 Boc기를 제거하였다. 10% DIEA(1×1분)를 사용하여 펩타이드 수지를 중화한 후, 15% 에타올아민/15% 물/50% DMF 용액으로 2×30분 동안 처리하여 Trp 측쇄 상의 포르밀기를 제거하였다. DMF 및 DCM을 사용하여 펩타이드 수지를 세척하고 감압 하에서 건조하였다. 펩타이드 수지를 0℃ 하에 1㎖의 아니솔 및 디티오트레이톨(24 mg)을 함유하는 10 ㎖ HF 내에서 75분간 교반하여 최종 절단(cleavage)을 수행하였다. 질소를 환류시켜 HF를 제거하였다. 에테르(6×10㎖)를 사용하여 잔류물을 세척하고, 4N HOAc(6×10㎖)를 사용하여 상기 잔류물을 추출하였다.

역상 VYDAC$^{(R)}$ C_{18} 칼럼(Nest Group, Southborough, MA)을 사용하여 제조용 역상 고압 액체 크로마토그래피(HPLC) 상에서 수계 추출물 내의 펩타이드 혼합물을 정제하였다. 직선 구배(105분에 걸쳐 20% 내지 50%의 B 용액)를 사용하여 10 ㎖/분의 저속으로 칼럼을 용리시켰다(A 용액 = 0.1%의 TFA를 함유하는 물; B 용액 = 0.1%의 TFA를 함유하는 아세토니트릴). 단편들을 수집하여 분석용 HPLC 상에서 조사하였다. 순수한 산물을 함유하는 것들을 조합하여 동결 건조하였다. 135 mg의 백색 고체가 얻어졌으며, 분석용 HPLC 분석을 기준으로 한 순도는 98.6%이었다. 전기 분무 질량 분광계(MS(ES))S 분석에 의한 분자량은 3339.7였다(이는 계산 분자량인 3339.7 g과 일치한다).

실시예 2

$((N_{\alpha}\text{-HEPES-His})^{7}, Aib^{8,35})hGLP-1(7-36)NH_2$

다음과 같은 방식으로 표제 화합물(HEPES는 4(-(2-하이드록시에틸)-1-피페라진-에탄설폰산)임)을 합성하였다: 실시예 1의 절차에 따라 MBHA 수지(0.20 mmol) 상에서 $(Aib^{8,35})hGLP-1(7-36)NH_2$를 조립한 후, 펩타이드 수지를 100% TFA로 처리하고(2×2분), DMA 및 DCM를 사용하여 세척하였다. 그런 다음, DMF 내의 10% DIEA(1×1분)를 사용하여 펩타이드 수지를 2분 동안 중화하였다. DMA 및 DCM를 사용하여 세척한 후, DMF 내의 2-클로로-1-에탄술포닐 클로라이드(0.23 mmol) 및 DIEA(0.7 mmol)로 수지를 1시간 동안 처리하였다. DMF 및 DCM을 사용하여 펩타이드 수지를 세척

하고, 1.2 mmol의 2-하이드록시에틸피페라진으로 2시간 동안 처리하였다. DMF 및 DCM을 사용하여 펩타이드 수지를 세척하고, 상이한 반응물질((1) DMF 내의 20% 머캡토에탄올/10% DIEA 및 (2) 15% 에탄올아민/15% 물/70% DMF)로 처리하여 수지로부터 펩타이드의 최종 HF가 절단되기 전에 His 측쇄 상의 DNP기 및 Trp 측쇄 상의 포르밀기를 제거하였다.

실시예 3

$((N_{\alpha}\text{-HEPA-His})^{7}, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$

2-클로로-1-에탄술포닐 클로라이드 대신 2-브로모아세트산 무수물이 사용된 것을 제외하고는, 실질적으로 실시예 2에 기재된 절차에 따라 표제 화합물(HEPA는 4(-(2-하이드록시에틸)-1-피페라진아세틸)임)을 합성하였다.

실시예 4

$(Aib^{8}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$

실질적으로 실시예 1에 기재된 절차에 따라 적절하게 보호된 아미노산을 사용하여 표제 화합물을 합성하였다. MS(ES)의 분자량은 3325.7이었으며, 계산 분자량은 3325.8이고, 순도는 99%이고, 수율은 85 mg이었다.

본 발명의 그 밖의 다른 화합물들은 원하는 펩타이드에 따라 적절하게 보호된 아미노산을 사용하는 것을 제외하고는 상기 실시예 1에서의 $(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$ 합성 절차와 실질적으로 동일한 방식으로 합성하였다.

실시예 5

$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{\varepsilon}\text{-테트라데카노일}))hGLP\text{-}1(7\text{-}36)NH_2$

본 실시예에 사용된 Boc 아미노산은 Fmoc-Lys(Boc)-OH가 사용된 것을 제외하고는 실시예 1에서 $(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$ 합성에 사용된 아미노산과 동일한 아미노산이다. 교반기 상에서 1번 아미노산 잔기를 수지에 수동으로 커플링하였다. 2.5 mmol의 Fmoc-Lys(Boc)-OH를 4㎖의 DMF 내의 0.5N HBTU에 용해시키고, 상기 용액에 1㎖의 DIEA를 첨가하였다. 혼합물을 약 2분 동안 교반한 다음, 거기에 0.2 mmol의 MBHA 수지(치환율 = 0.91 mmol/g)를 첨가하였다. 혼합물을 약 1시간 동안 교반한 후, DMF를 사용하여 수지를 세척하고, 100% TFA로 2×2분 동안 처리하여 Boc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하였다. 4㎖ DMF 내의 HBTU(2.0 mmol) 및 DIEA(1.0 ㎖)를 사용하여 미리스트산(2.5 mmol)을 사전 활성화하고, Fmoc-Lys-수지에 커플링하였다. 커플링에 소요된 시간은 약 1시간이었다. DMF를 사용하여 수지를 세척하고, DMF 내의 25% 피페리딘으로 2×20분 동안 처리하여 Fmoc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하고, 펩타이드 합성기의 반응용기로 옮겼다. 다음 단계의 펩타이드 합성 및 정제 과정은 실시예 1에서 $(Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$ 합성에 사용된 과정과 동일하였다. 43.1 mg의 표제 화합물이 백색 고체 형태로 얻어졌다. 분석용 HPLC 분석을 기준으로 한 순도는 98%이었다. 전기 분무 질량 분광계 분석에 의한 분자량은 3577.7이었으며, 이는 계산 분자량인 3578.7과 일치하는 값이다.

실시예 6-8

실질적으로 실시예 5에 기재된 절차에 따라 실시예 5에 사용된 미리스트산 대신 적절하게 보호된 아미노산 및 적합한 산을 사용하여 실시예 6, 7 및 8을 합성하였다.

실시예 6: $(Aib^{8,35}, Arg^{26}, Lys^{34}(N_{\varepsilon}\text{-테트라카노일}))hGLP\text{-}1(7\text{-}36)NH_2$; 수율 = 89.6 mg; MS(ES) = 3577.2, 계산 MW = 3578.7; 순도 = 96%.

실시예 7: $(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{\varepsilon}\text{-테트라데카노일}))hGLP\text{-}1(7\text{-}38)NH_2$; 수율 = 63.3 mg; MS(ES) = 3818.7, 계산 MW = 3819.5; 순도 = 96%.

실시예 8: $(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{\varepsilon}\text{-데카노일}))hGLP\text{-}1(7\text{-}36)NH_2$; 수율 = 57.4 mg; MS(ES) = 3521.5, 계산 MW = 3522.7; 순도 = 96%; 산 = 데카노산.

실시예 5에 기재된 절차와 유사한 방식으로 $Lys(N_{\varepsilon}\text{-알카노일})$ 잔기를 함유하는 본 발명의 다른 화합물을 합성하였다. 여기서, 펩타이드 내의 $Lys(N_{\varepsilon}\text{-알카노일})$ 잔기로는 Fmoc-Lys(Boc)-OH 아미산이 사용되었고, Lys 잔기로는 Boc-Lys(2ClZ)-OH 아미노산이 사용되었다. $Lys(N_{\varepsilon}\text{-알카노일})$ 잔기가 C-말단에 존재하지 않는 경우에는, 우선적으로 펩타이드 합성기 상의 수지 상에서 $Lys(N_{\varepsilon}\text{-알카노일})$ 잔기 바로 앞의 펩타이드 단편이 조립된다. Aldrich Chemical Co., Inc 사(Milwaukee, WI, USA)로부터 원하는 알카노일에 대응하는 적합한 산, 예를 들면 옥탄산, 데칸산, 라우르산 및 팔미트산을 구입하였다.

실시예 9

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-(2-도데칸술포닐))hGLP-1(7-36)NH_2

본 실시예의 합성에 사용된 Boc 아미노산은 실시예 5의 합성에 사용된 것과 동일한 것이다. 교반기 상에서 1번 아미노산 잔기를 수지에 수동으로 커플링하고, 2.5 mmol의 Fmoc-Lys(Boc)-OH를 4㎖의 DMF 내의 0.5N HBTU에 용해시켰다. 상기 용액에 1㎖의 DIEA를 첨가한 뒤, 혼합물을 약 2분 동안 교반하였다. 상기 용액에 0.2 mmol의 MBHA 수지(치환율 = 0.91 mmol/g)를 첨가하고, 혼합물을 약 1시간 동안 교반하였다. DMF를 사용하여 수지를 세척하고, 수지를 100% TFA로 2×2분 동안 처리하여 Boc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하고, 여기에 4㎖ DMF 내의 0.25 mmol 1-도데칸술포닐 클로라이드 및 1㎖의 DIEA를 첨가하였다. 혼합물을 약 2시간 동안 교반한 후, DMF를 사용하여 수지를 세척하고, DMF 내의 25% 피페리딘으로 2×20분 동안 처리하여 Fmoc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하고, 펩타이드 합성기의 반응용기로 옮겼다. 펩타이드에 대한 나머지 합성 및 정제 과정은 실시예 1에 기재된 것과 동일하다.

실시예 9에 기재된 절차와 유사한 방식으로 Lys(N_{ε}-알킬술포닐) 잔기를 함유하는 본 발명의 다른 화합물을 합성하였다. 펩타이드 내의 Lys(N_{ε}-알킬술포닐) 잔기로는 Fmoc-Lys(Boc)-OH 아미노산이 사용되었고, Lys 잔기로는 Boc-Lys(2ClZ)-OH 아미노산이 사용되었다. Lys(N_{ε}-알킬술포닐) 잔기가 C-말단에 존재하지 않는 경우에는, 우선적으로 펩타이드 합성기 상의 수지 상에서 Lys(N_{ε}-알킬술포닐) 잔기 바로 앞의 펩타이드 단편이 조립된다. Lancaster Synthesis Inc.사(Windham, NH, USA)로부터 적합한 알킬술포닐 클로라이드, 예를 들면 1-옥탄술포닐 클로라이드, 1-데칸술포닐 클로라이드, 1-도데칸술포닐 클로라이드, 1-헥사데칸술포닐 클로라이드 및 1-옥타데실술포닐 클로라이드를 구입하였다.

실시예 10

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))

hGLP-1(7-36)NH_2

본 실시예에 사용된 Boc 아미노산은 실시예 5의 합성에 사용된 것과 동일한 아미노산이다. 교반기 상에서 1번 아미노산 잔기를 수지에 수동으로 커플링하였다. 2.5 mmol의 Fmoc-Lys(Boc)-OH를 4㎖의 DMF 내의 0.5N HBTU에 용해시키고, 상기 용액에 1㎖의 DIEA를 첨가하였다. 혼합물을 약 2분 동안 교반한 다음, 그 용액에 0.2 mmol의 MBHA 수지(치환율 = 0.91 mmol/g)를 첨가하였다. 혼합물을 약 1시간 동안 교반한 후, DMF를 사용하여 수지를 세척하고, 100% TFA로 2×2분 동안 처리하여 Boc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하였다. 4㎖의 DMF 내의 HBTU(2.0 mmol) 및 DIEA(1.0 ㎖)를 사용하여 2-브로모아세트산(2.5 mmol)을 약 2분 동안 사전 활성화하고, 수지에 첨가하였다. 혼합물을 약 10분 동안 교반하고 DMF를 사용하여 세척하였다. 그런 다음, 수지를 4㎖ DMF 내의 1.2 mmol 피페리딘으로 2시간 동안 처리하였다. DMF를 사용하여 수지를 세척하고, 2 mmol의 1-이오도테트라데칸을 약 4시간 동안 처리하였다. DMF를 사용하여 수지를 세척한 후, 4㎖ DMF 내의 3 mmol 아세트산 무수물 및 1㎖ DIEA로 약 0.5시간 동안 처리하였다. DMF를 사용하여 수지를 세척하고, DmF 내의 25% 피페라진으로 2×20분 동안 처리하였다. DMF를 사용하여 수지를 세척하고, 펩타이드 합성기의 반응요기로 옮겨 합성을 계속하였다. 펩타이드에 대한 나머지 합성 및 정제 과정은 실시예 1에 기재된 과정과 동일하다.

실시예 10의 합성 절차와 유사한 방식으로 Lys(N_{ε}-2-(4-알킬-1-피페라진)-아세틸)) 잔기를 함유하는 본 발명의 다른 화합물을 합성하였다. 펩타이드 내의 Lys(N_{ε}-2-(4-알킬-1-피페라진)-아세틸)) 잔기로는 Fmoc-Lys(Boc)-OH 아미노산이 사용되었고, Lys 잔기로는 Boc-Lys(2ClZ)-OH 아미노산이 사용되었다. 알킬화 단계 중의 Lys(N_{ε}-2-(4-알킬-1-피페라진)-아세틸)) 잔기로는 해당 요오도알칸이 사용되었다. Lys(N_{ε}-2-(4-알킬-1-피페라진)-아세틸)) 잔기가 C-말단에 존재하지 않는 경우에는, 우선적으로 펩타이드 합성기 상의 수지 상에서 Lys(N_{ε}-2-(4-알킬-1-피페라진)-아세틸)) 잔기 바로 앞의 펩타이드 단편이 조립된다.

실시예 11

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(1-(4-테트라데실-1-피페라진)))

hGLP-1(7-36)NH_2

본 실시예에 사용된 Boc 아미노산은 36번 위치에 Fmoc-Asp(O-tBu)-OH가 사용되는 것을 제외하고는 실시예 5의 합성에 사용된 것과 동일한 아미노산이다. 교반기 상에서 1번 아미노산 잔기를 수지에 수동으로 커플링하였다. 2.5 mmol의 Fmoc-Asp(O-tBu)-OH를 4㎖의 DMF 내의 0.5N HBTU에 용해시키고, 상기 용액에 1㎖의 DIEA를 첨가하였다. 혼합물을 약 2분 동안 교반한 다음, 그 용액에 0.2 mmol의 MBHA 수지(치환율 = 0.91 mmol/g)를 첨가하였다. 혼합물을 약 1시간 동안 교반한 후, DMF를 사용하여 수지를 세척하고, 100% TFA로 2×15분 동안 처리하여 Boc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하고, 4㎖ DMF 내의 HBTU(0.6 mmol) 및 DIEA(1㎖)로 약 15분 동안 처리하였다. 반응 혼합물에 0.6 mmol의 피페라진을 첨가하고, 혼합물을 약 1시간 동안 교반하였다. DMF를 사용하여 수지를 세척하고, 3 mmol의 1-요오도테트라데칸으로 약 4시간 동안 처리하였다. DMF를 사용하여 수지를 세척한 후, 4㎖ DMF 내의 3 mmol 아세트산 무수물 및 1㎖ DIEA로 약 0.5시간 동안 처리하였다. 수지를 DMF 내의 25% 피페리딘으로 2×20분 동안 처리하여 Fmoc 보호기를 제거하였다. 수지를 DMF로 세척하고 펩타이드 합성기의 반응용기로 옮겨 합성을 계속하였다. 펩타이드에 대한 나머지 합성 및 정제 과정은 실시예 1에 기재된 과정과 동일하다.

실시예 11의 합성 절차와 유사한 방식으로 Asp(1-(4-알킬피페라진)) 또는 Glu(1-(4-알킬피페라진)) 잔기를 포함하는 발명의 다른 화합물들을 합성하였다. 펩타이드 내의 Asp(1-(4-알킬피페라진)) 또는 Glu(1-(4-알킬피페라진)) 잔기로는 Fmoc-Asp(O-tBu)-OH 또는 Fmoc-Glu(O-tBu)-OH 아미노산이 사용되었고, Asp 또는 Glu 잔기로는 Asp(OcHex)-OH 또는 Boc-Glu(OcHex)-OH 아미노산이 사용되었다. 알킬화 단계 중의 Lys(N_{ε}-2-(4-알킬-1-피페라진)-아세틸)) 잔기로는 해당 요오도알칸이 사용되었다. Asp(1-(4-알킬피페라진)) 또는 Glu(1-(4-알킬피페라진)) 잔기가 C-말단에 존재하지 않는 경우에는, 우선적으로 펩타이드 합성기 상의 수지 상에서 Asp(1-(4-알킬피페라진)) 또는 Glu(1-(4-알킬피페라진)) 잔기 바로 앞의 펩타이드 단편이 조립된다.

실시예 12

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-테트라데실아미노))hGLP-1(7-36)NH_2

본 실시예에 사용된 Boc 아미노산은 실시예 5에 사용된 것과 동일한 아미노산이다. 교반기 상에서 1번 아미노산 잔기를 수지에 수동으로 커플링하였다. 2.5 mmol의 Fmoc-Asp(O-tBu)-OH를 4㎖의 DMF 내의 0.5N HBTU에 용해시켰다. 상기 용액에 1㎖의 DIEA를 첨가하였다. 혼합물을 약 2시간 동안 교반한 다음, 그 용액에 0.2 mmol의 MBHA 수지(치환율 = 0.91 mmol/g)를 첨가하였다. 혼합물을 약 1시간 동안 교반한 후, DMF를 사용하여 수지를 세척하고, 100% TFA로 2×15분 동안 처리하여 t-Bu 보호기를 제거하였다. DMF를 사용하여 수지를 세척하고, 4㎖의 DMF 내의 HBTU(0.6 mmol) 및 DIEA(1㎖)로 약 15분 동안 처리하였다. 반응 혼합물에 0.6 mmol의 테트라데칸아민을 첨가하고, 혼합물을 약 1시간 동안 교반하였다. DMF를 사용하여 수지를 세척하고, DMF 내의 25% 피페라진으로 약 2×20분 동안 처리하여 Fmoc 보호기를 제거하였다. DMF를 사용하여 수지를 세척하고 펩타이드 합성기의 반응기로 옮겨 합성을 계속하였다. 펩타이드에 대한 나머지 합성 및 정제 과정은 실시예 1에 기재된 과정과 동일하다.

실시예 12의 합성 절차와 유사한 방식으로 Asp(1-알킬아미노) 또는 Glu(1-알킬아미노) 잔기를 함유하는 본 발명의 다른 화합물들을 합성하였다. 펩타이드 내의 Asp(1-알킬아미노) 또는 Glu(1-알킬아미노) 각각의 잔기로는 Fmoc-Asp(O-tBu)-OH 또는 Fmoc-Glu(O-tBu)-OH 아미노산이 사용되었고, Asp 또는 Glu 각각의 잔기로는 Boc-Asp(OcHex)-OH 또는 Boc-Glu(OcHex)-OH 아미노산이 사용되었다. Asp(1-알킬아미노) 또는 Glu(1-알킬아미노) 잔기가 C-말단에 존재하지 않는 경우에는, 우선적으로 펩타이드 합성기 상의 수지 상에서 Asp(1-알킬아미노) 또는 Glu(1-알킬아미노) 잔기 바로 앞의 펩타이드 단편이 조립된다.

실시예 13

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라도데카노일), β-Ala^{37})hGLP-1(7-36)OH

사용된 Boc 아미노산은 (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라도데카노일))hGLP-1(7-36)NH_2(실시예 5)의 합성에 사용된 것과 동일한 아미노산이다. 270 mg의 Boc-β-Ala-PAM 수지(Novabiochem사, San Diego, California 소재, 치환율 = 0.74 mmol/g)가 사용되었다. 교반기 상에서 100% TFA로 2×2분 동안 처리하여 Boc-β-Ala-PAM 수지 상의 Boc 보호기를 제거하였다. 나머지 합성 및 정제 과정은 실시예 5에서의 과정과 동일하였다. 83.0 mg의 표제 화합물이 백색 고체 형태로 얻어졌다. 분석용 HPLC 분석을 기준으로 한 순도는 99%이었다. 전기 분무 질량 분광계 분석에 의한 분자량은 3650.5이었으며, 이는 계산 분자량인 3650.8과 일치하는 값이다.

실시예 14

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라도데카노일))hGLP-1(7-36)OH

사용된 Boc 아미노산은 (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라도데카노일))hGLP-1(7-36)NH_2(실시예 5)의 합성에 사용된 것과 동일한 아미노산이다. DMF(4 ㎖) 내의 HBTU(2.0 mmol), HoBT(2.0 mmol) 및 DIEA(2.5 ㎖)를 사용하여 Fmoc-Lys(Boc)-OH(2.5 mmol)을 약 2분간 사전 활성화하고, 교반기 상에서 상기 아미노산을 235 mg의 PAM 수지(Chem-Impex사, Wood Dale, IL 소재; 치환율 = 0.85 mmol/g)에 수동으로 커플링하였다. 커플링에 소요된 시간은 약 8시간이었다. 나머지 합성 및 정제 과정은 실시예 5에서의 과정과 동일하였다. 전기 분무 질량 분광계 분석에 의한 분자량은 3579.15이었으며, 이는 계산 분자량인 3579.5와 일치하는 값이다.

실시예 14의 합성 절차와 유사한 방식으로 Lys(N_{ε}-알카노일) 잔기를 함유하는 본 발명의 hGLP-1(7-36)OH, hGLP-1(7-37)OH 및 hGLP-1(7-38)OH의 다른 유사체를 합성하였다. 펩타이드 내의 Lys(N_{ε}-알카노일) 잔기로는 Fmoc-Lys(Boc)-OH 아미노산이 사용되었고, Lys 잔기로는 Boc-Lys(2ClZ)-OH 아미노산이 사용되었다.

실시예 366

(Aib^{8}, β-Arg^{35}, Aec^{37})hGLP-1(7-37)NH_2

반응용기 내의 MBHA 수지(0.2 mmol, 치환율 = 0.91 mmol/g), Fmoc-Aec-OH(0.40 g, 0.829 mmol), HBTU(1.5 ㎖ @ DMF 내 0.5M) 및 DIEA(0.5㎖) 혼합물을 실온 하의 교반기 상에서 4시간 동안 교반하였다. DMF를 사용하여 수지를 세척하고, DMF 내의 25% 피페라진으로 2×20분 동안 처리하였다. 이어서, DMF 및 DCM을 사용하여 수지를 세척한 뒤, 펩타

이드 합성기의 반응용기로 옮기고 실시예 1에 기재된 절차에 따라 나머지 펩타이드의 조립을 계속하였다. 정제 과정 또한 실시예 1에 기재된 과정과 동일하였다. 전기 분무 질량 분광계 분석에 의한 분자량은 3494.8이었으며, 이는 계산 분자량인 3494.99과 일치하는 값이고, 순도는 93%이고, 수율은 79.1 mg이었다.

실시예 367

$(Aib^{8}, \beta\text{-}Arg^{35}, Aec^{37})hGLP\text{-}1(7\text{-}38)NH_2$

실질적으로 실기예 366에 기재된 절차에 따라 실시예 367을 합성하였다. MS는 3551.7이고, 계산 MS는 3552.04이고, 순도는 97%이고, 수율은 97.4 mg이었다.

실시예 368

$(Aib^{8}, \beta\text{-}Arg^{35}, Aec^{37,38})hGLP\text{-}1(7\text{-}38)NH_2$

반응용기 내의 MBHA 수지(0.2 mmol, 치환율 = 0.91 mmol/g), Fmoc-Aec-OH(0.289 g, 0.6 mmol), HBTU(1.12 ㎖ @ DMF 내 0.5M) 및 DIEA(0.4㎖) 혼합물을 실온 하의 교반기 상에서 2시간 동안 교반하였다. DMF를 사용하여 수지를 세척하고, DMF 내의 30% 피페라진으로 2×15분 동안 처리하였다. 이어서, DMF를 사용하여 수지를 세척하였다. 반응용기에 Fmoc-Aec-OH(0.289 g, 0.6 mmol), HBTU(1.12 ㎖ @ DMF 내 0.5M) 및 DIEA(0.4㎖)을 첨가하였다. 반응 혼합물을 실용에서 2시간 동안 교반한 뒤, DMF를 사용하여 수지를 세척하고, DMF 내의 30% 피페라진으로 2×15분 동안 처리하였다. DMF 및 DCM을 사용하여 수지를 세척한 후, 펩타이드 합성기의 반응용기로 옮기고 실시예 1에 기재된 절차에 따라 나머지 펩타이드의 조립을 계속하였다. 정제 과정 또한 실시예 1에 기재된 과정과 동일하였다. 전기 분무 질량 분광계 분석에 의한 분자량은 3663.9이었으며, 이는 계산 분자량인 3664.26과 일치하는 값이고, 순도는 100%이고, 수율은 75.3 mg이었다.

실시예 369

$(Aib^{8}, Arg^{26,34}, \beta\text{-}Ala^{35}, Lys^{36}(N_{\varepsilon}\text{-}Aec\text{-}데카노일))hGLP\text{-}1(7\text{-}36)NH_2$

반응용기 내의 MBHA 수지(0.2 mmol, 치환율 = 0.91 mmol/g), Boc-Lys(Fmoc)-OH(1.17 g, 2.5 mmol), HBTU(4 ㎖ @ DMF 내 0.5M) 및 DIEA(1㎖) 혼합물을 실온 하의 교반기 상에서 10분 동안 교반하였다. DMF를 사용하여 수지를 세척하고, DMF 내의 25% 피페라진으로 2×15분 동안 처리하였다. 이어서, DMF를 사용하여 수지를 세척하였다. 반응용기에 Fmoc-Aec-OH(0.289 g, 0.6 mmol), HBTU(1.12 ㎖ @ DMF 내 0.5M) 및 DIEA(0.4㎖)을 첨가하였다. 반응 혼합물을 실용에서 2시간 동안 교반한 뒤, DMF를 사용하여 수지를 세척하고, DMF 내의 30% 피페라진으로 2×15분 동안 처리하였다. DMF를 사용하여 수지를 세척한 후, 데칸산(431 mg, 2.5 mmol), HBTU(4 ㎖ @ DMF 내 0.5M) 및 DIEA(1 ㎖)의 혼합물로 10분 동안 처리하였다. DMF를 사용하여 수지를 세척하고, 100% TFA로 2×2분 동안 처리하였다. DMF 및 DCM을 사용하여 수지를 세척하고, 펩타이드 합성기의 반응용기로 옮겨서 실시예 1에 기재된 절차에 따라 나머지 펩타이드의 조립을 계속하였다. 정제 과정 또한 실시예 1에 기재된 과정과 동일하였다. 전기 분무 질량 분광계 분석에 의한 분자량은 3677.0이었으며, 이는 계산 분자량인 3677.25와 일치하는 값이고, 순도는 97.6%이고, 수율은 44.8 mg이었다.

상기에 기재된 적합한 방법에 따라 하기 실시예들을 제조하였다:

실시예 15: $(Aib^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 16: $(\beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 17: $((N_{\alpha}\text{-}Me\text{-}His)^{7}, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 18: $((N_{\alpha}\text{-}Me\text{-}His)^{7}, Aib^{8}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 19: $((N_{\alpha}\text{-}Me\text{-}His)^{7}, Aib^{8,35}, Arg^{26,34})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 20: $((N_{\alpha}\text{-}Me\text{-}His)^{7}, Aib^{8}, Arg^{26,34}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 21: $(Aib^{8}, A6c^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 22: $(Aib^{8}, A5c^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 23: $(Aib^{8}, D\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

실시예 24: (Aib^{8,35}, A6c^{32})hGLP-1(7-36)NH_2;

실시예 25: (Aib^{8,35}, A5c^{32})hGLP-1(7-36)NH_2;

실시예 26: (Aib^{8,35}, Glu^{23})hGLP-1(7-36)NH_2;

실시예 27: (Aib^{8,24,35})hGLP-1(7-36)NH_2;

*실시예 28: (Aib^{8,30,35})hGLP-1(7-36)NH_2;

실시예 29: (Aib^{8,25,35})hGLP-1(7-36)NH_2;

실시예 30: (Aib^{8,35}, A6c^{16,20})hGLP-1(7-36)NH_2;

실시예 31: (Aib^{8,35}, A6c^{16,29,32})hGLP-1(7-36)NH_2;

실시예 32: (Aib^{8,35},A6c^{20,32})hGLP-1(7-36)NH_2;

실시예 33: (Aib^{8,35}, A6c^{20})hGLP-1(7-36)NH_2;

실시예 34: (Aib^{8,35},Lys^{25})hGLP-1(7-36)NH_2;

실시예 35: (Aib^{8,24,35}, A6c^{20})hGLP-1(7-36)NH_2;

실시예 36: (Aib^{8,35}, A6c^{29,32})hGLP-1(7-36)NH_2;

실시예 37: (Aib^{8,24,35},A6c^{29,32})hGLP-1(7-36)NH_2;

실시예 38: (Aib^{8,35}, A6c^{12})hGLP-1(7-36)NH_2;

실시예 39: (Aib^{8,35}, Cha^{20})HGLP-1(7-36)NH_2;

실시예 40: (Aib^{8,35}, A6c^{33})hGLP-1(7-36)NH_2;

실시예 41: (Aib^{8,35} A6c^{20,32})hGLP-1(7-36)NH_2;

실시예 42: (Aib^{8}, A6c^{16,20}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 43: (Aib^{8,35}, β-Ala^{22})hGLP-1(7-36)NH_2;

실시예 44: (Aib^{8,22,35})hGLP-1(7-36)NH_2;

실시예 45: (Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

실시예 46: (Aib^{8,24,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

실시예 47: (Aib^{8,24,25,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

실시예 48: (Aib^{8,24,25,35}, A6c^{18,20,32}, Glu^{23})hGLP-1(7-36)NH_2;

실시예 49: (Aib^{8}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 50: (Aib^{8}, A5c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 51: (Aib^{8}, Glu^{23}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 52: (Aib^{8,24}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 53: (Aib^{8,30}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 54: (Aib^{8,25}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 55: (Aib^{8}, A6c^{16,20}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 56: (Aib^{8}, A6c^{16,29,32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 57: (Aib^{8}, A6c^{20,32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 58: (Aib^{8}, A6c^{20}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 59: (Aib^{8}, Lys^{25}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 60: (Aib^{8,24}, A6c^{20}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 61: (Aib^{8}, A6c^{29,32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 62: (Aib^{8,24}, A6c^{29,32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 63: (Aib^{8}, A6c^{12}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 64: (Aib^{8}, Cha^{20}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 65: (Aib^{8}, A6c^{33}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 66: (Aib^{8}, A6c^{20,32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 67: (Aib^{8}, β-Ala^{22,35})hGLP-1(7-36)NH_2;

실시예 68: (Aib^{8,22}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 69: (Aib^{8}, Glu^{23}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 70: (Aib^{8,24}, Glu^{23}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 71: (Aib^{8,24}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 72: (Aib^{8,24,25}, Glu^{23}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 73: (Aib^{8,24,25}, A6c^{16,20,32}, Glu^{23}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 74: (Aib^{8,35}, D-Alg^{36})hGLP-1(7-36)NH_2;

실시예 75: (Aib^{8,35}, D-Lys^{36})hGLP-1(7-36)NH_2;

실시예 76: (Aib^{8}, β-Ala^{35}, D-Alg^{36})hGLP-1(7-36)NH_2;

실시예 77: (Aib^{8}, β-Ala^{35}, D-Lys^{36})hGLP-1(7-36)NH_2;

실시예 78: (Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

실시예 79: (Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 80: (Aib^{8,35}, Arg^{25,28,34})hGLP-1(7-36)NH_2;

실시예 81: (Aib^{8}, Arg^{25,26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 82: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-36) OH;

실시예 83: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-37)OH;

실시예 84: (Aib^{8,35,37}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-37)OH;

실시예 85: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일), D-Ala^{37})hGLP-1 (7-37)OH;

실시예 86: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-테트라데카노일))hGLP-1(7-38)OH;

실시예 87: (Aib^{8,35}, Arg^{26,34}, β-Ala^{38}, Lys^{36}(N_ε-테트라데카노일))hGLP-1 (7-38)OH;

실시예 88: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-테트라데카노일))hGLP-1(7-38)OH;

실시예 89: (Aib^{8}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일), β-Ala^{37})hGLP-1 (7-37)OH;

실시예 90: (Aib^{8,37}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-37)OH;

실시예 91: (Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)OH;

실시예 92: (Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)NH_2;

*실시예 93: (Aib^{8}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일), D-Ala^{37})hGLP-1(7-37) OH;

실시예 94: (Aib^{8,37}, Arg^{26,34}, Lys^{38}(N_ε-테트라데카노일))hGLP-1(7-38)OH;

실시예 95: (Aib^{8}, Arg^{26,34}, β-Ala^{37}, Lys^{38}(N_ε-테트라데카노일))hGLP-1 (7-38)OH;

실시예 96: (Aib^{8,35}, Lys^{26}(N_ε-옥타노일))hGLP-1(7-36)NH_2;

실시예 97: (Aib^{8,35}, Lys^{26}(N_ε-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 98: (Aib^{8,35}, Lys^{26}(N_ε-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 99: (Aib^{8}, Lys^{26}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 100: (Aib^{8}, Lys^{26}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 101: (Aib^{8}, Lys^{26}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 102: (Aib^{8,35}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 103: (Aib^{8,35}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 104: (Aib^{8,35}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 105: (Aib^{8,35}, Lys^{26}(N_{ε}-데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 106: (Aib^{8,35}, Lys^{25}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 107: (Aib^{8,35}, Lys^{25}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1 (7-36)NH_2;

실시예 108: (Aib^{8,35}, Lys^{25}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1 (7-36)NH_2;

실시예 109: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 110: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 111: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 112: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 113: (Aib^{8}, Lys^{26}(N_{ε}-옥타노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 114: (Aib^{8}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 115: (Aib^{8}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 116: (Aib^{8}, Lys^{26}(N_{ε}-데카노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 117: (Aib^{8,35}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 118: (Aib^{8,35}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 119: (Aib^{8,35}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 120: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 121: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 122: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 123: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 124: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 125: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 126: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 127: (Aib^{8,35}, Lys^{25}, Arg^{26},Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 128: (Aib^{8,35}, Lys^{25},Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 129: (Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 130: (Aib^{8,35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 131: (Aib^{8,35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 132: (Aib^{8,35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 133: (Aib^{8,35}, Arg^{26}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 134: (Aib^{8,35}, Arg^{26}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 135: (Aib^{8,35}, Arg^{26}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 136: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 137: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 138: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

실시예 139: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

실시예 140: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38)NH_2;

실시예 141: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

실시예 142: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

실시예 143: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

실시예 144: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38) NH_2;

실시예 145: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

실시예 146: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

실시예 147: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

실시예 148: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

실시예 149: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

실시예 150: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

실시예 151: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38) NH_2;

실시예 152: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

실시예 153: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 154: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1 (7-36)NH_2;

실시예 155: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-38) NH_2;

실시예 156: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 157: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 158: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

실시예 159: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

실시예 160: (Aib^{8}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 161: (Aib^{8}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 162: (Aib^{8}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 163: (Aib^{8}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 164: (Aib^{8}, Glu^{23}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 165: (Aib^{8}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 166: (Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 167: (Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 168: (Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 169: (Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 170: (Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 171: (Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 172: (Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 173: (Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-데카노일), β-Ala^{35})hGLP-1(7-38)NH_2;

실시예 174: (Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36) NH_2;

실시예 175: (Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 176: (Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 177: (Aib^{8}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 178: (Aib^{8}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 179: (Aib^{8}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 180: (Aib^{8}, Arg^{26}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 181: (Aib^{8}, Arg^{26}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 182: (Aib^{8}, Arg^{26}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 183: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 184: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1 (7-36)NH_2;

실시예 185: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 186: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 187: (Aib^{8}, Lys^{25}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1 (7-36)NH_2;

실시예 188: (Aib^{8}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 189: (Aib^{8}, Lys^{25}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1 (7-36)NH_2;

실시예 190: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 191: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1 (7-36)NH_2;

실시예 192: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 193: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 194: (Aib^{8,35}, Lys^{26}(N_{ε}-옥타노일), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

실시예 195: (Aib^{8,35}, Lys^{26}(N_{ε}-테트라데카노일), A6c^{32}, Arg^{34})hGLP-1(7-36) NH_2;

실시예 196: (Aib^{8,35}, Lys^{26}(N_{ε}-헥사데카노일), A6c^{32}, Arg^{34})hGLP-1(7-36) NH_2;

실시예 197: (Aib^{8,35}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 198: (Aib^{8,35}, A6c^{32}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 199: (Aib^{8,35}, A6c^{32}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 200: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 201: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 202: (Aib^{8,35}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 203: (Aib^{8,35}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 204: (Aib^{8,35}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 205: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 206: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 207: (Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 208: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 209: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 210: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1 (7-36)NH_2;

실시예 211: (Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 212: (Aib^{8,24,35}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 213: (Aib^{8,24,35}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 214: (Aib^{8,24,35}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 215: (Aib^{8,24,35}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 216: (Aib^{8,24,35}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 217: (Aib^{8,24,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 218: (Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 219: (Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 220: (Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 221:(Aib^{8,24,35}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 222: (Aib^{8,35}, Glu^{23}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 223: (Aib^{8,35}, Glu^{23}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36) NH_2;

실시예 224: (Aib^{8,35}, Glu^{23}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36) NH_2;

실시예 225: (Aib^{8,35}, Glu^{23}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 226: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 227: (Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 228: (Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 229: (Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 230: (Aib^{8,35}, Glu^{23}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 231: (Aib^{8,35}, Glu^{23}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 232: (Aib^{8,35}, Glu^{23}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 233: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 234: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1 (7-36)NH_2;

실시예 235: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 236: (Aib^{8,30,35}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 237: (Aib^{8,30,35}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 238: (Aib^{8,30,35}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

실시예 239: (Aib^{8,30,35}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 240: (Aib^{8,30,35}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 241: (Aib^{8,30,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 242: (Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 243: (Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

실시예 244: (Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 245: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

실시예 246: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

실시예 247: (Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

실시예 248: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1 (7-36)NH_2;

실시예 249: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일)) hGLP-1(7-36)NH_2;

실시예 250: (Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

실시예 251: (Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일)) hGLP-1(7-36)NH_2;

실시예 252: (Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일)) hGLP-1(7-36)NH_2;

실시예 253: (Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일)) hGLP-1(7-36)NH_2;

실시예 254: (Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))GLP-1 (7-36)NH_2;

실시예 255: (Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일)) hGLP-1(7-36)NH_2;

실시예 256: (Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일)) hGLP-1(7-36)NH_2;

실시예 257: ((N_{α}-HEPES-His)^{7}, Aib^{35})hGLP-1(7-36)NH_2;

실시예 258: ((N_{α}-HEPES-His)^{7}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 259: ((N_{α}-HEPES-His)^{7}, Aib^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 260: ((N_{α}-HEPA-His)^{7}, Aib^{35})hGLP-1(7-36)NH_2;

실시예 261: ((N_{α}-HEPA-His)^{7}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 262: ((N_{α}-HEPA-His)^{7}, Aib^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 263: ((N_{α}-테트라데카노일-His)^{7}, Aib^{35})hGLP-1(7-36)NH_2;

실시예 264: ((N_{α}-테트라데카노일-His)^{7}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 265: ((N_{α}-테트라데카노일-His)^{7}, Aib^{8,35})hGLP-1(7-36)NH_2;

실시예 266: ((N_{α}-테트라데카노일-His)^{7}, Aib^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 267: ((N_{α}-테트라데카노일-His)^{7}, Arg^{26,34}, Aib^{35})hGLP-1(7-36)NH_2;

실시예 268: ((N_{α}-테트라데카노일-His)^{7}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 269: ((N_{α}-테트라데카노일-His)^{7}, Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

실시예 270: ((N_{α}-테트라데카노일-His)^{7}, Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 271: ((N_{α}-테트라데카노일-His)^{7}, Arg^{25,26,34}, β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 272: ((N_{α}-테트라데카노일-His)^{7}, Aib^{8,35}, Arg^{25,26,34})hGLP-1(7-36)NH_2;

실시예 273: ((N_{α}-테트라데카노일-His)^{7}, Aib^{8}, Arg^{25,26,34}, β-Ala^{35})hGLP-1 (7-36)NH_2;

실시예 274: (Aib^{8,35}, Lys^{26}(N_{ε}-옥탄술포닐), Arg^{34})hGLP-1(7-36)NH_2;

실시예 275: (Aib^{8,35}, Lys^{26}(N_{ε}-도데칸술포닐), Arg^{34})hGLP-1(7-36)NH_2;

실시예 276: (Aib^{8,35}, Lys^{26}(N_{ε}-헥사데칸술포닐), Arg^{34})hGLP-1(7-36)NH_2;

실시예 277: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-옥탄술포닐))hGLP-1(7-36)NH_2;

실시예 278: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-도데칸술포닐))hGLP-1(7-36)NH_2;

실시예 279: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데칸술포닐))hGLP-1(7-36)NH_2;

실시예 280: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥탄술포닐))hGLP-1(7-36)NH_2;

실시예 281: (Aib^{8,35}, Arg^{26,34}, Lys^{34}(N_{ε}-헥사데칸술포닐))hGLP-1(7-36)NH_2;

실시예 282: (Aib^{8,35}, Asp^{26}(1-(4-데실피페라진)), Arg^{34})hGLP-1(7-36)NH_2;

실시예 283: (Aib^{8,35}, Asp^{26}(1-(4-도데실피페라진)), Arg^{34})hGLP-1(7-36)NH_2;

실시예 284: (Aib^{8,35}, Asp^{26}(1-(4-테트라데실피페라진)), Arg^{34})hGLP-1(7-36) NH_2;

실시예 285: (Aib^{8,35}, Asp^{26}(1-(4-헥사데실피페라진)), Arg^{34})hGLP-1(7-36) NH_2;

실시예 286: (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

실시예 287: (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-도데실피페라진)))hGLP-1(7-36)NH_2;

실시예 288: (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-테트라데실피페라진)))hGLP-1(7-36) NH_2;

실시예 289: (Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-헥사데실피페라진)))hGLP-1(7-36) NH_2;

실시예 290: (Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

실시예 291: (Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-도데실피페라진)))hGLP-1(7-36) NH_2;

실시예 292: (Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-헥사데실피페라진)))hGLP-1(7-36) NH_2;

실시예 293: (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38)NH_2;

실시예 294: (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38) NH_2;

실시예 295: (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 296: (Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1(7-38) NH_2;

실시예 297: (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38) NH_2;

실시예 298: (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38) NH_2;

실시예 299: (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 300: (Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 301: (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

실시예 302: (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-도데실피페라진)))hGLP-1(7-36) NH_2;

실시예 303: (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-테트라데실피페라진)))hGLP-1 (7-36)NH_2;

실시예 304: (Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-헥사데실피페라진)))hGLP-1 (7-36)NH_2;

실시예 305: (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

실시예 306: (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-도데실피페라진)))hGLP-1(7-36) NH_2;

실시예 307: (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-테트라데실피페라진)))hGLP-1 (7-36)NH_2;

실시예 308: (Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-헥사데실피페라진)))hGLP-1(7-36) NH_2;

실시예 309: (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-데실피페라진)))hGLP-1(7-36) NH_2;

실시예 310: (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-도데실피페라진)))hGLP-1(7-36) NH_2;

실시예 311: (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-테트라데실피페라진)))hGLP-1 (7-36)NH_2;

실시예 312: (Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-헥사데실피페라진)))hGLP-1 (7-36)NH_2;

실시예 313: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38) NH_2;

실시예 314: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38) NH_2;

실시예 315: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 316: (Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 317: (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 318: (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 319: (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 320: (Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1 (7-38)NH_2;

실시예 321: (Aib^{8,35}, Arg^{26,34}, Glu^{36}(1-도데실아미노))hGLP-1(7-36)NH_2;

실시예 322: (Aib^{8,35}, Glu^{26}(1-도데실아미노), Arg^{34})hGLP-1(7-36)NH_2;

실시예 323: (Aib^{8,35}, Arg^{26}, Glu^{34}(1-도데실아미노))hGLP-1(7-36)NH_2;

실시예 324: (Aib^{8,35,37}, Arg^{26,34}, Glu^{38}(1-도데실아미노))hGLP-1(7-38)NH_2;

실시예 325: (Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 326: (Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-도데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 327: (Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 328: (Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 329: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 330: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-도데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 331: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 332: (Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 333: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 334: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-(2-(4-도데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 335: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 336: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-38)NH_2;

실시예 337: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-도데실-1-피페라진)-아세틸))) hGLP-1(7-38)NH_2;

실시예 338: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 339: (Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 340: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 341: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 342: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 343: (Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 344: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_ε-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 345: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(2-(4-도데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 346: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 347: (Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_ε-(2-(4-헥사데실-1-피페라진)- 아세틸)))hGLP-1(7-36)NH_2;

실시예 348: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_ε-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 349: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 350: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 351: (Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 352: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-36)NH_2;

실시예 353: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 354: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 355: (Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

실시예 356: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸))) hGLP-1(7-38)NH_2;

실시예 357: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 358: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 359: (Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 360: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 361: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 362: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 363: (Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

실시예 364: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

실시예 375: (Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

실시예 370: (Aib^{8,35}, Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2;

실시예 371: (Aib^{8,35}, Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2;

실시예 372: (Aib^{8,35}, Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2;

실시예 373: (Aib^{8,17,35})hGLP-1(7-36)NH_2;

실시예 374: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39) NH_2;

실시예 375: (Gly^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 376: (Ser^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 377: (Aib^{8}, Glu^{22,23}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 378: (Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2;

실시예 379: (Aib^{8}, Lys^{18}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 380: (Aib^{8}, Leu^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 381: (Aib^{8}, Lys^{33}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 382: (Aib^{8}, Lys^{18}, Leu^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 383: (Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2;

실시예 384: (Aib^{8}, β-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2;

실시예 385: (Aib^{8,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 386: (Aib^{8,27}, β-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2;

실시예 387: (Aib^{8,27}, β-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH_2;

실시예 388: (Aib^{8}, Lys^{18,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 399: (Aib^{8}, Lys^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 390: (Aib^{8}, β-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

실시예 391: (Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 392: (Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

실시예 393: (Aib^{8}, β-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

실시예 394: (Aib^{8}, Phe^{31}, β-Ala^{35})hGLP-1(7-36)NH_2;

실시예 395: (Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

실시예 396: (Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

실시예 397: (Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

실시예 398: (Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

실시예 399: (Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

실시예 400: (Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

실시예 401: (Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

실시예 402: (Aib^{8,35}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 403: (Aib^{8,35}, Arg^{34}, Lys^{26}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

실시예 404: (Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-도데카노일))hGLP-1(7-36)NH_2;

실시예 405: (Aib^{8}, B-Ala^{35}, Ser^{37}(O-데카노일))hGLP-1(7-37)NH_2;

실시예 406: (Aib^{8,27}, β-Ala^{35,37}, Arg^{38}, Lys^{39}(N_{ε}-옥타노일))hGLP-1(7-39) NH_2;

실시예 407: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_{ε}-옥타노일))hGLP-1(7-37)NH_2;

실시예 408: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_{ε}-데카노일))hGLP-1(7-37)NH_2;

실시예 409: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_{ε}-테트라데카노일))hGLP-1 (7-37)NH_2;

실시예 410: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_{ε}-도데카노일))hGLP-1(7-37) NH_2; 또는

실시예 411: (Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_{ε}-도데카노일))hGLP-1(8-37) NH_2.

예시된 화합물들의 대표적인 샘플링에 대한 물리학적 데이터를 하기 표 1에 기재하였다.

< 표 1 >

실시예 번호	예상 분자량	분자량 MS(ES)	순도 (HPLC)
24	3351.8	3352.2	88%
26	3340.17	3340.9	99%
27	3353.81	3353.9	99%
29	3353.81	3353.9	99%
45	3352.6	3352.5	97%
51	3326.74	3326.6	99%
78	3395.81	3395.5	96%
136	3494	3494	99%
364	3523.02	3523.6	99%
365	3580.13	3580.3	95%
369	3677.25	3677	97%
370	3692.28	3692.4	98%
371	3807.37	3807.3	98%
372	3579.11	3579.7	97.90%
373	3337.81	3338.5	94%
374	3779.3	3779.5	94%
375	3297.7	3297.5	99%
376	3327.7	3327.4	98%
377	3398.8	3398.7	97.50%
378	3311.6	3311	93%
379	3366.85	3366.5	97%
380	3309.8	3309.4	99%
381	3354.8	3354.5	97.70%
382	3350.9	3350.3	97.20%
383	3311.73	3310.7	92%
384	3481.95	3481.3	94.30%
385	3281.76	3281.6	98%
386	3509.02	3509.1	99.40%
387	3665.2	3665.1	99%
388	3365.91	3365	97%
389	3324.79	3324.2	95%
390	3539	3539.2	93%
391	3381.74	3381.3	97%
392	3410.89	3409.8	99%
393	3481.95	3481.1	90%
394	3286.76	3286.2	99.20%
395	3300.76	3299.4	93%
396	3350.81	3349.4	99%
397	3400.87	3400.1	99%
398	3406.84	3406.4	99%
399	3356.77	3356.6	99%
400	3384.87	3384.43	94%
401	3400.87	3401.3	99%
402	3466.03	3466.9	97.40%
403	3522.05	3522.06	93%
404	3550.11	3550.2	98%
405	3567.09		99%
406	3763.38	3763.2	95%
407	3636.15	3635.8	99%
408	3664.21	3663.3	99%
409	3720.32	3719.5	99%
410	3692.27	3691.7	99%
411	3555.13	3554.4	99%

발명의 효과

본 발명은 글루카곤형 펩타이드-1의 펩타이드 유사체, 제약학적으로 허용 가능한 이들의 염, 상기 유사체를 사용하여 포유류를 치료하는 방법 및 이러한 치료방법에 유용한, 상기 유사체를 포함하는 약제 조성물에 관한 것이다.

(57) 청구의 범위

청구항 1.

화학식 (I)을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염:

(R^2R^3)-A^7-A^8-A^9-A^{10}-A^{11}-A^{12}-A^{13}-A^{14}-A^{15}-A^{16}-A^{17}-A^{18}-A^{19}-A^{20}-A^{21}-A^{22}-A^{23}-A^{24}-A^{25}-A^{26}-

A^{27}-A^{28}-A^{29}-A^{30}-A^{31}-A^{32}-A^{33}-A^{34}-A^{35}-A^{36}-A^{37}-A^{38}-A^{39}-R^1 (I)

상기 식에서,

A^7은 L-His, Ura, Paa, Pta, Amp, Tma-His 또는 탈아미노(des-amino)-His이거나 결실이고;

A^8은 Ala, D-Ala, Aib, Acc, N-Me-Ala, N-Me-D-Ala 또는 N-Me-Gly이고;

A^9는 Glu, N-Me-Glu, N-Me-Asp 또는 Asp이고;

A^{10}은 Gly, Acc, β-Ala 또는 Aib이고;

A^{11}은 Thr 또는 Ser이고;

A^{12}는 Phe, Acc, Aic, Aib, 3-Pal, 4-Pal, β-Nal, Cha, Trp 또는 X^1-Phe이고;

A^{13}은 Thr 또는 Ser이고;

A^{14}는 Ser 또는 Aib이고;

A^{15}는 Asp 또는 Glu이고;

A^{16}은 Val, Acc, Aib, Leu, Ile, Tle, Nle, Abu, Ala 또는 Cha이고;

A^{17}은 Ser 또는 Thr이고;

A^{18}은 Ser 또는 Thr이고;

A^{19}는 Tyr, Cha, Phe, 3-Pal, 4-Pal, Acc, β-Nal 또는 X^1-Phe이고;

A^{20}은 Leu, Acc, Aib, Nle, Ile, Cha, Tle, Val, Phe 또는 X^1-Phe이고;

A^{21}은 Glu 또는 Asp이고;

A^{22}는 Gly, Acc, β-Ala, Glu 또는 Aib이고;

A^{23}은 Gln, Asp, Asn 또는 Glu이고;

A^{24}는 Ala, Aib, Val, Abu, Tle 또는 Acc이고;

A^{25}는 Ala, Aib, Val, Abu, Tle, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-$N(R^{10}R^{11})$)-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이고;

A^{26}은 Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이고;

A^{27}은 Glu, Asp, Leu, Aib 또는 Lys이고;

A^{28}은 Phe, Pal, β-Nal, X^1-Phe, Aic, Acc, Aib, Cha 또는 Trp이고;

A^{29}는 Ile, Acc, Aib, Leu, Nle, Cha, Tle, Val, Abu, Ala 또는 Phe이고;

A^{30}은 Ala, Aib 또는 Acc이고;

A^{31}은 Trp, β-Nal, 3-Pal, 4-Pal, Phe, Acc, Aib 또는 Cha이고;

A^{32}는 Leu, Acc, Aib, Nle, Ile, Cha, Tle, Phe, X^1-Phe 또는 Ala이고;

A^{33}은 Val, Acc, Aib, Leu, Ile, Tle, Nle, Cha, Ala, Phe, Abu, Lys 또는 X^1-Phe이고;

A^{34}는 Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이고;

A^{35}는 Gly, β-Ala, D-Ala, Gaba, Ava, HN-$(CH_2)_m$-C(O), Aib, Acc 또는 D-아미산이고;

A^{36}은 L- 또는 D-Arg, D- 또는 L-Lys, D- 또는 L-hArg, D- 또는 L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$)-C(O) 또는 HN-CH($(CH_2)_e$-X^3)-C(O)이거나 결실이고;

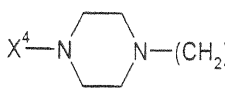
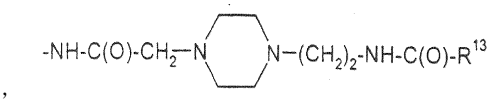
A^{37}은 Gly, β-Ala, Gaba, Ava, Aib, Acc, Ado, Arg, Asp, Aun, Aec, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O) 또는 D-아미노산이거나 결실이고;

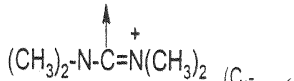
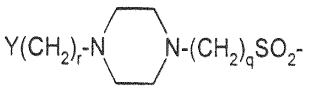
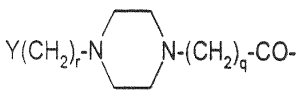
A^{38}은 D- 또는 L-Lys, D- 또는 L-Arg, D- 또는 L-hArg, D- 또는 L-Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O), HN-CH($(CH_2)_e$-X^3)-C(O), Ava, Ado 또는 Aec이거나 결실이고;

A^{39}는 D- 또는 L-Lys, D- 또는 L-Arg, HN-CH($(CH_2)_n R^{10}R^{11}$))-C(O), Ava, Ado, 또는 Aec이고;

각각의 경우에 대하여 X^1은 (C_1-C_6)알킬, OH 및 할로(halo)기로 이루어지는 군으로부터 독립적으로 선택되고;

R^1은 OH, NH_2, (C_1-C_{30})알콕시 및 NH-X^2-CH_2-Z^0이고, 여기서 X^2는 (C_1-C_{12})탄화수소 모이어티이고, Z^0은 H, OH, $C0_2H$ 및 $CONH_2$로 이루어지는 군으로부터 선택되고;

X^3은 ,  및 -C(O)-NHR^{12}로 이루어지는 군으로부터 선택되며, 여기서 X^4는 각각의 경우에 대하여 -C(O)-, -NH-C(O)- 및 -CH_2-으로 이루어지는 군으로부터 독립적으로 선택되고, f는 각각의 경우에 대해 독립적으로 1 내지 29를 포함하는 정수 중 하나이고;

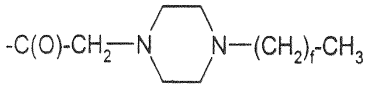
각각의 R^2 및 R^3은 H, (C_1-C_{30})알킬, (C_2-C_{30})알케닐, 페닐(C_1-C_{30})알킬, 나프틸(C_1-C_{30})알킬, 하이드록시(C_1-C_{30})알킬, 하이드록시(C_2-C_{30})알케닐, 하이드록시페닐(C_1-C_{30})알킬 및 하이드록시나프틸(C_1-C_{30})알킬로 이루어지는 군으로부터 독립적으로 선택되거나; R^2와 R^3 중 하나는 , (C_1-, (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, C(O)X^5,  및  로 이루어지는 군으로부터 선택되며; 상기 식에서 Y는 H, OH

및 NH_2로 이루어지는 군으로부터 선택되고; r은 0 내지 4이고; q는 0 내지 4이고; X^5는 (C_1-C_{30})알킬, (C_2-C_{30})알케닐, 페닐(C_1-C_{30})알킬, 나프틸(C_1-C_{30})알킬, 하이드록시(C_1-C_{30})알킬, 하이드록시(C_2-C_{30})알케닐, 하이드록시페닐(C_1-C_{30})알킬 및 하이드록시나프틸(C_1-C_{30})알킬로 이루어지는 군으로부터 선택되고;

e는 각각의 경우에 대하여 독립적으로 1 내지 4를 포함하는 정수 중 하나이고;

m은 각각의 경우에 대하여 독립적으로 5 내지 24를 포함하는 정수 중 하나이고;

n은 각각의 경우에 대하여 독립적으로 1 내지 5를 포함하는 정수 중 하나이고;

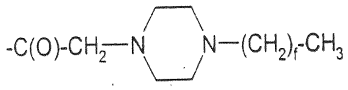
R^{10} 및 R^{11} 각각은 각각의 경우에 대하여 H, (C_1-C_{30})알킬, (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, -C((NH)(NH_2)) 및 

으로 이루어지는 군으로부터 독립적으로 선택되고;

R^{12} 및 R^{13} 각각은 각각의 경우에 대하여 독립적으로 (C_1-C_{30})알킬이고;

단,

A^7이 Ura, Paa 또는 Pta인 경우, R^2 및 R^3은 결실이고;

R^{10}이 (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, -C((NH)(NH_2)) 및 

로 이루어지는 군으로부터 선택되는 경우, R^{11}은 H 또는 (C_1-C_{30})알킬이고;

(i) 화학식(Ⅰ)의 화합물 중 적어도 하나의 아미노산은 hGLP-1(7-36, -37 또는 -38)NH_2 또는 hGLP-1(7-36, -37 및 -38)OH의 천연 서열과 동일하지 않고;

(ii) 화학식(Ⅰ)의 화합물은 hGLP-1(7-36, -37 또는 -38)NH_2 또는 hGLP-1(7-36, -37 또는 -38)OH—여기서 한 위치가 Ala로 치환됨—의 유사체가 아니고;

(iii) 화학식(Ⅰ)의 화합물은 ($Arg^{26,34}$, Lys^{38})hGLP-1(7-38)-E, (Lys^{26}(N_ε-알카노일))hGLP-1(7-36, -37 또는 -38)-E, (Lys^{34}(N_ε-알카노일))hGLP-1(7-36, -37 또는 38)-E, ($Lys^{26,34}$-비스(N_ε-알카노일))hGLP-1(7-36, -37 및 -38)-E, (Arg^{26}, Lys^{34}(N_ε-알카노일))hGLP-1(8-36, -37 또는 -38)-E, ($Arg^{26,34}$, Lys^{36}(N_ε-알카노일)) hGLP-1(7-36, -37 또는 -38)-E 또는 ($Arg^{26,34}$, Lys^{38}(N_ε-알카노일))hGLP-1 (7-38)-E—여기서 E는 -OH 및 -NH_2임—가 아니고;

(iv) 화학식(Ⅰ)의 화합물은 Z^1-hGLP-1(7-36, -37 또는 -38)-OH, Z^1-hGLP-1(7-36, -37 또는 -38)-NH_2가 아니며, 이때 Z^1은 다음으로 이루어지는 군으로부터 선택되고:

(a) (Arg^{26}), (Arg^{34}), ($Arg^{26,34}$), (Lys^{36}), (Arg^{26}, Lys^{36}), (Arg^{34}, Lys^{36}), (D-Lys^{36}), (Arg^{36}), (D-Arg^{36}), ($Arg^{26,34}$, Lys^{36}) 또는 ($Arg^{26,36}$, Lys^{34});

(b) (Asp^{21});

(c) (Aib^8), (D-Ala^8) 및 (Asp^9) 중 적어도 하나; 및

(d) (Tyr^7), (N-아실-His^7), (N-알킬-His^7), (N-아실-D-His^7) 및 (N-알킬-D-His^7);

(v) 화학식(Ⅰ)의 화합물은 (a) 내지 (d) 군에 기재된 임의의 두 치환기의 조합체가 아니고;

(vi) 화학식(Ⅰ)의 화합물은 (N-Me-Ala^8)hGLP-1(8-36 또는 -37), (Glu^{15}) hGLP-1(7-36 또는 -37), (Asp^{21})hGLP-1(7-36 및 -37) 및 (Phe^{31})hGLP-1(7-36 및 -37)임.

청구항 2.

제1항에 있어서,

A^{11}은 Thr이고; A^{13}은 Thr이고; A^{15}는 Asp이고; A^{17}은 Ser이고; A^{18}은 Ser이고; A^{21}은 Glu이고; A^{23}은 Gln 또는 Glu이고; A^{27}은 Glu이고; A^{31}은 Trp인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

청구항 3.

제2항에 있어서,

A^{9}는 Glu, N-Me-Glu 및 N-Me-Asp로 이루어지는 군으로부터 선택되고; A^{12}는 Phe, Acc, β-Nal 및 Aic로 이루어지는 군으로부터 선택되고; A^{16}은 Val, Acc 및 Aib로 이루어지는 군으로부터 선택되고; A^{19}는 Tyr이고; A^{20}은 Leu, Acc 및 Cha로 이루어지는 군으로부터 선택되고; A^{24}는 Ala, Aib 및 Acc로 이루어지는 군으로부터 선택되고; A^{25}는 Ala, Aib, Acc, Lys, Arg, hArg, Orn, HN-CH($(CH_2)_n$-N($R^{10}R^{11}$))-C(O) 및 HN-CH($(CH_2)_e$-X^3)-C(O)로 이루어지는 군으로부터 선택되고; A^{28}은 Phe이고; A^{29}는 Ile 또는 Acc이고; A^{30}은 Ala 또는 Aib이고; A^{32}는 Leu, Acc 및 Cha로 이루어지는 군으로부터 선택되고; A^{33}은 Val 또는 Acc인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

청구항 4.

제3항에 있어서,

A^{8}은 Ala, D-Ala, Aib, A6c, A5c, N-Me-Ala, N-Me-D-Ala 및 N-Me-Gly로 이루어지는 군으로부터 선택되고; A^{10}은 Gly이고; A^{12}는 Phe, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{16}은 Val, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{20}은 Leu, A6c, A5c 및 Cha로 이루어지는 군으로부터 선택되고; A^{22}는 Gly, β-Ala 및 Aib로 이루어지는 군으로부터 선택되고; A^{24}는 Ala 또는 Aib이고; A^{29}는 Ile, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{32}는 Leu, A6c, A5c 및 Cha로 이루어지는 군으로부터 선택되고; A^{33}은 Val, A6c 및 A5c로 이루어지는 군으로부터 선택되고; A^{35}는 Aib, β-Ala, Ado, A6c, A5c, D-Arg 및 Gly로 이루어지는 군으로부터 선택되고; A^{37}은 Gly, Aib, β-Ala, Ado 및 D-Ala로 이루어지는 군으로부터 선택되나 결실인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

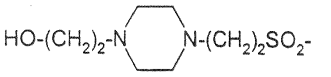
청구항 5.

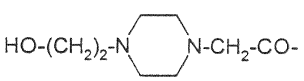
제4항에 있어서,

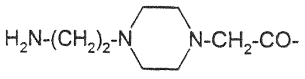
각각의 경우에 대하여 X^4는 -C(O)-이고; e는 각각의 경우에 대하여 독립적으로 1 또는 2이고; R^1은 OH 또는 NH_2인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

청구항 6.

제5항에 있어서,

R^2는 H이고 R^3은 (C_1-C_{30})알킬, (C_2-C_{30})알케닐, (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐, 

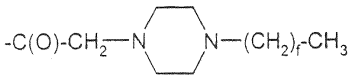
,


또는 

인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

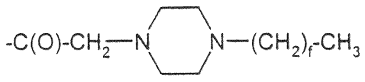
청구항 7.

제5항에 있어서,

R^{10}은 (C_1-C_{30})아실, (C_1-C_{30})알킬술포닐 또는  이고, R^{11}은 H인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

청구항 8.

제7항에 있어서,

R^{10}이 (C_4-C_{20})아실, (C_4-C_{20})알킬술포닐 도는  인 화합물 또는 제약학적으로 허용 가능한 이들의 염.

청구항 9.

제1항에 있어서,

상기 화합물이 하기 화학식들로 이루어지는 군으로부터 선택되는 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염:

($(N_\alpha$-HEPES-HiS)^7, Aib^{8,35})hGLP-1(7-36)NH_2,

($(N_\alpha$-HEPA-HiS)^7, Aib^{8,35})hGLP-1(7-36)NH_2,

(Aib^8, β-Ala^{35})hGLP-1(7-36)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_ε-테트라데카노일)hGLP-1(7-36)NH_2,

(Aib^{8,35}, Ala^{26}, Lys^{34}(N_ε-테트라데카노일)hGLP-1(7-36)NH_2,

(Aib^{8,35,37}, Ala^{26,34}, Lys^{38}(N_ε-테트라데카노일)hGLP-1(7-38)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_ε-데카노일)hGLP-1(7-36)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_ε-도데칸술포닐)hGLP-1(7-36)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(1-(4-테트라데실-피페라진)))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(1-테트라데실아미노))hGLP-1(7-36)NH_2,

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_ε-테트라데카노일), β-Ala^{37})hGLP-1(7-37)-OH, 및

(Aib^{8,35}, Ala^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-36)-OH.

청구항 10.

제9항에 있어서,

상기 화합물이 하기 화학식들로 이루어지는 군으로부터 선택되는 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염:

$(Aib^{8}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$,

$(Aib^{8,35}, Arg^{26}, Lys^{34}(N_{\varepsilon}\text{-}테트라데카노일)hGLP\text{-}1(7\text{-}36)NH_2$,

$(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{\varepsilon}\text{-}테트라데카노일)hGLP\text{-}1(7\text{-}38)NH_2$,

$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{\varepsilon}\text{-}데카노일)hGLP\text{-}1(7\text{-}36)NH_2$, 및

$(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{\varepsilon}\text{-}테트라데카노일), \beta\text{-}Ala^{37})hGLP\text{-}1(7\text{-}37)\text{-}OH$.

청구항 11.

유효량의 제1항에 따른 화합물 또는 제약학적으로 허용 가능한 이들의 염 및 제약학적으로 허용 가능한 담체 또는 희석제를 포함하는 약제 조성물.

청구항 12.

GLP-1 수용체로부터 아고니스트 작용(agonist effect)를 유도하기 위한 유효량의 제1항에 따른 화합물 또는 제약학적으로 허용 가능한 이들의 염을 포함하는 약제 조성물.

청구항 13.

유효량의 제1항에 따른 화합물 또는 제약학적으로 허용 가능한 이들의 염을 포함하는 I형 당뇨병, II형 당뇨병, 비만증, 글루카곤종, 기도의 분비 장애, 대사 장애, 관절염, 골다공증, 중추신경계 질환, 협착증, 신경변성 질환, 신부전, 충혈성 심부전, 신증, 경화, 폐수종, 고혈압, 및 음식물 섭취에 있어 감소가 요구되는 질환으로 이루어지는 군으로부터 선택되는 질병을 치료하기 위한 약제 조성물.

청구항 14.

제13항에 있어서,

상기 질병이 I형 당뇨병 또는 II형 당뇨병인 치료방법.

청구항 15.

제1항에 있어서,

상기 화합물이 하기 화학식들로 이루어지는 군으로부터 선택되는 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염:

$(Aib^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(\beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N_{\alpha}\text{-}Me\text{-}His)^{7}, Aib^{8,35})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N_{\alpha}\text{-}Me\text{-}His)^{7}, Aib^{8}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N_{\alpha}\text{-Me-His})^{7}, Aib^{8,35}, Arg^{26,34})hGLP\text{-}1(7\text{-}36)NH_2$;

$((N_{\alpha}\text{-Me-His})^{7}, Aib^{8}, Arg^{26,34}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, A6c^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, A5c^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, D\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A5c^{32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, Glu^{23})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,24,35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,30,35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,25,35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{16,20})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{16,29,32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35},A6c^{20,32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{20})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35},Lys^{25})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,24,35}, A6c^{20})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{29,32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,24,35},A6c^{29,32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{12})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, Cha^{20})HGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, A6c^{33})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}\ A6c^{20,32})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8}, A6c^{16,20}, \beta\text{-}Ala^{35})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,35}, \beta\text{-}Ala^{22})hGLP\text{-}1(7\text{-}36)NH_2$;

$(Aib^{8,22,35})hGLP-1(7-36)NH_2$;

$(Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2$;

$(Aib^{8,24,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2$;

$(Aib^{8,24,25,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2$;

$(Aib^{8,24,25,35}, A6c^{18,20,32}, Glu^{23})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A5c^{32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, Glu^{23}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8,24}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8,30}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8,25}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{16,20}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{16,29,32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{20,32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{20}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, Lys^{25}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8,24}, A6c^{20}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{29,32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8,24}, A6c^{29,32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{12}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, Cha^{20}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{33}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, A6c^{20,32}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

$(Aib^{8}, \beta-Ala^{22,35})hGLP-1(7-36)NH_2$;

$(Aib^{8,22}, \beta-Ala^{35})hGLP-1(7-36)NH_2$;

(Aib^{8}, Glu^{23}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, Glu^{23}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24}, Glu^{23}, A6c^{32}, Lys^{34}(N_ε-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24,25}, Glu^{23}, A6c^{32}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,24,25}, A6c^{16,20,32}, Glu^{23}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, D-Alg^{36})hGLP-1(7-36)NH_2;

(Aib^{8,35}, D-Lys^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, D-Alg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, D-Lys^{36})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,28,34})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-36)OH;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-37)OH;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-37)OH;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일), D-Ala^{37})hGLP-1(7-37)OH;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-테트라데카노일))hGLP-1(7-38)OH;

(Aib^{8,35}, Arg^{26,34}, β-Ala^{38}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-38)OH;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-테트라데카노일))hGLP-1(7-38)OH;

(Aib^{8}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일), β-Ala^{37})hGLP-1(7-37)OH;

(Aib^{8,37}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일))hGLP-1(7-37)OH;

(Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)OH;

(Aib^{8,35}, Arg^{26,34}, Ado^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, Lys^{36}(N_ε-테트라데카노일), D-Ala^{37})hGLP-1(7-37)OH;

(Aib^{8,37}, Arg^{26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38)OH;

(Aib^{8}, Arg^{26,34}, β-Ala^{37}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38)OH;

(Aib^{8,35}, Lys^{26}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-옥타노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{26}(N_{ε}-데카노일), Arg^{34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26},Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25},Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-옥타노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-테트라데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-38)NH_2;

(Aib^{8}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, Lys^{34}(N_{ε}-데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{25,26}, Lys^{34}(N_{ε}-데카노일), β-Ala^{35})hGLP-1(7-38)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일), β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{25}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-옥타노일), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-테트라데카노일), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{26}(N_{ε}-헥사데카노일), A6c^{32}, Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Lys^{26}(N_{ε}-옥타노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Lys^{26}(N_{ε}-테트라데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Lys^{26}(N_{ε}-헥사데카노일), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Arg^{26}, Lys^{34}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Arg^{26}, Lys^{34}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Arg^{26}, Lys^{34}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,30,35}, Arg^{26,34}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

(Aib^{8,24,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-테트라데카노일))hGLP-1(7-36) NH_2;

(Aib^{8,24,30,35}, Glu^{23}, Arg^{26,34}, A6c^{32}, Lys^{36}(N_{ε}-헥사데카노일))hGLP-1(7-36) NH_2;

($(N_{\alpha}$-HEPES-His)^7, Aib^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-HEPES-His)^7, β-Ala^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-HEPES-His)^7, Aib^8, β-Ala^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-HEPA-His)^7, Aib^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-HEPA-His)^7, β-Ala^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-HEPA-His)^7, Aib^8, β-Ala^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-테트라데카노일-His)^7, Aib^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-테트라데카노일-His)^7, β-Ala^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-테트라데카노일-His)^7, Aib^{8,35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-테트라데카노일-His)^7, Aib^8, β-Ala^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-테트라데카노일-His)^7, Arg^{26,34}, Aib^{35})hGLP-1(7-36)NH_2;

($(N_{\alpha}$-테트라데카노일-His)^7, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

((N$_{\alpha}$-테트라데카노일-His)^{7}, Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH$_2$;

((N$_{\alpha}$-테트라데카노일-His)^{7}, Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH$_2$;

((N$_{\alpha}$-테트라데카노일-His)^{7}, Arg^{25,26,34}, β-Ala^{35})hGLP-1(7-36)NH$_2$;

((N$_{\alpha}$-테트라데카노일-His)^{7}, Aib^{8,35}, Arg^{25,26,34})hGLP-1(7-36)NH$_2$;

((N$_{\alpha}$-테트라데카노일-His)^{7}, Aib^{8}, Arg^{25,26,34}, β-Ala^{35})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Lys^{26}(N$_{\varepsilon}$-옥탄술포닐), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Lys^{26}(N$_{\varepsilon}$-도데칸술포닐), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Lys^{26}(N$_{\varepsilon}$-헥사데칸술포닐), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$_{\varepsilon}$-옥탄술포닐))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$_{\varepsilon}$-도데칸술포닐))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N$_{\varepsilon}$-헥사데칸술포닐))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N$_{\varepsilon}$-옥탄술포닐))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Lys^{34}(N$_{\varepsilon}$-헥사데칸술포닐))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Asp^{26}(1-(4-데실피페라진)), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Asp^{26}(1-(4-도데실피페라진)), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Asp^{26}(1-(4-테트라데실피페라진)), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Asp^{26}(1-(4-헥사데실피페라진)), Arg^{34})hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-도데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-테트라데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26}, Asp^{34}(1-(4-헥사데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-도데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Asp^{36}(1-(4-헥사데실피페라진)))hGLP-1(7-36)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38)NH$_2$;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-도데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-테트라데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Asp^{26}(1-(4-헥사데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-도데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-테트라데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Asp^{34}(1-(4-헥사데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-도데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-테트라데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{36}(1-(4-헥사데실피페라진)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-도데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-테트라데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Asp^{38}(1-(4-헥사데실피페라진)))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Glu^{36}(1-도데실아미노))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{26}(1-도데실아미노), Arg^{34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Glu^{34}(1-도데실아미노))hGLP-1(7-36)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Glu^{38}(1-도데실아미노))hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{26}, Lys^{34}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-38) NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-38) NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35,37}, Arg^{26,34}, Lys^{38}(N_ε-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,34}, Lys^{26}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26}, Lys^{34}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-36) NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{36}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-36)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1(7-38) NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-도데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-테트라데실-1-피페라진)-아세틸)))hGLP-1(7-38)NH_2;

(Aib^{8,35,37}, Arg^{25,26,34}, Lys^{38}(N_{ε}-(2-(4-헥사데실-1-피페라진)-아세틸)))hGLP-1 (7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

(Aib^{8,35}, Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2;

(Aib^{8,35}, Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2;

(Aib^{8,17,35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH_2;

(Gly^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Ser^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{22,23}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Leu^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{33}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, Leu^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH_2;

(Aib^{8}, Lys^{18,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Phe^{31}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N_ε-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-도데카노일))hGLP-1(7-36)NH_2;

(Aib^{8}, B-Ala^{35}, Ser^{37}(O-데카노일))hGLP-1(7-37)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38}, Lys^{39}(N_ε-옥타노일))hGLP-1(7-39)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-옥타노일))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-데카노일))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-테트라데카노일))hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-도데카노일))hGLP-1(7-37)NH_2; 및

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-도데카노일))hGLP-1(8-37)NH_2.

청구항 16.

제15항에 있어서,

상기 화합물이 하기 화학식들로 이루어지는 군으로부터 선택되는 화학식을 가지는 화합물 또는 제약학적으로 허용 가능한 이들의 염:

(Aib^{8,35}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23})hGLP-1(7-36)NH_2;

(Aib^{8,24,35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Glu^{23}, A6c^{32})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{23}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-옥타노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-데카노일))hGLP-1(7-36)OH;

(Aib^{8,35}, Lys^{25}, Arg^{26,34}, Lys^{36}(N_{ε}-데카노일))hGLP-1(7-36)OH;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{36}(N_{ε}-Aec-데카노일))hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Ava^{37}, Ado^{38})hGLP-1(7-38)NH_2;

(Aib^{8,35}, Arg^{26,34}, Asp^{37}, Ava^{38}, Ado^{39})hGLP-1(7-39)NH_2;

(Aib^{8,35}, Arg^{26,34}, Aun^{37})hGLP-1(7-37)NH_2;

(Aib^{8,17,35})hGLP-1(7-36)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, D-Asp^{37}, Ava^{38}, Aun^{39})hGLP-1(7-39)NH_2;

(Gly^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Ser^{8}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Glu^{22,33}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Gly^{8}, Aib^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Leu^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{33}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{18}, Leu^{27},β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{36})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, D-Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38,39})hGLP-1(7-39)NH_2;

(Aib^{8}, Lys^{18,27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, Lys^{27}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Arg^{38})hGLP-1(7-38)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, D-Arg^{35})hGLP-1(7-36)NH_2;

(Aib^{8}, β-Ala^{35}, Arg^{37})hGLP-1(7-37)NH_2;

(Aib^{8}, Phe^{31}, β-Ala^{35})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{28,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Nal^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Phe^{31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{19,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Nal^{12,31})hGLP-1(7-36)NH_2;

(Aib^{8,35}, Lys^{36}(N_ε-데카노일)hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{34}, Lys^{26}(N_ε-데카노일)hGLP-1(7-36)NH_2;

(Aib^{8,35}, Arg^{26,34}, Lys^{36}(N_ε-도데카노일)hGLP-1(7-36)NH_2;

(Aib^{8}, B-Ala^{35}, Ser^{37}(O-데카노일)hGLP-1(7-37)NH_2;

(Aib^{8,27}, β-Ala^{35,37}, Arg^{38}, Lys^{39}(N_ε-옥타노일)hGLP-1(7-39)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-옥타노일)hGLP-1(7-37)NH_2;

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-데카노일)hGLP-1(7-37)NH_2; 및

(Aib^{8}, Arg^{26,34}, β-Ala^{35}, Lys^{37}(N_ε-테트라데카노일)hGLP-1(7-37)NH_2.

청구항 17.

제1항 내지 제10항, 제15항 및 제16항 중 어느 한 항에 따른 화합물을 사용하여 질병 치료용 약제를 제조하는 방법.

청구항 18.

제17항에 있어서,

상기 질병이 I형 당뇨병, II형 당뇨병, 비만증, 글루카곤종, 기도의 분비 장애, 대사 장애, 관절염, 골다공증, 중추신경계 질환, 협착증 및 신경변성 질환으로 이루어지는 군으로부터 선택되는 방법.

<110> Societe de Conseils de Recherches et D'Applications Scientifiques S.A.S.

<120> ANALOGUES OF GLP-1

<130> P71419WO

<140> PCT/EP99/09660
<141> 1999-12-07

<150> 09/206,601
<151> 1998-12-07

<160> 363

<170> PatentIn Ver. 2.0

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<211> 30
<212> PRT
<213> Homo sapiens

<400> 1
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
             20   25   30

<210> 2
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 2
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 3
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazine-ethanesulfonic
acid)-histidine

<210>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 3
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 4
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazineacetyl)-histidine

<210>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
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<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 4
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 5

<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 5
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 6
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 6
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 7
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<222> (2)
<223> alpha-aminoisobutyric acid

<210>
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<222> (28)
<223> N-epsilon-tetradecanoyl-lysine

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 7
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
             20   25   30

<210> 8
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<210>
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<222> (32)...(32)

<223> Xaa = N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 8
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 9
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (30)
<223> N-epsilon-decanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 9
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 10
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (30)
<223> N-epsilon-dodecanesulfonyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 10
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 11
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (30)
<223> N-epsilon-(2-(4-tetradecyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 11
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 12
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (30)
<223> (1-(4-tetradecyl-piperazine)-acetyl)asparagine

<220>
<223> this sequence has an amidated c-terminus

<400> 12
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 13
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (30)
<223> (1-tetradecylamino)asparagine

<220>
<223> this sequence has an amidated c-terminus

<400> 13
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 14
<211> 31
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<210>
<221> MOD_RES
<222> (31)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 14
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa Xaa
20 25 30

<210> 15
<211> 30
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<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 15

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 16
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> 1-amino-1-cyclopentanecarboxylic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 16
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 17
<211> 31
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<213> Artificial Sequence

<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 17
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly
20 25 30

<210> 18
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<223> this sequence has an amidated c-terminus

<400> 18
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg

20 25 30

<210> 19
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<223> this sequence has an amidated c-terminus

<400> 19
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg Gly Arg
20 25 30

<210> 20
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N,N-tetramethylamidinohistidine

<220>
<223> this sequence has an amidated c-terminus

<400> 20
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 21
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> [125I]-3-iodotyrosine

<220>
<223> this sequence has an amidated c-terminus

<400> 21

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 22
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 22
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 23
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 23
His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 24
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>

<221> MOD_RES
<222> (1)
<223> N-alpha-methylhistidine

<210>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 24
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 25
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (1)
<223> N-alpha-methylhistidine

<210>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 25
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 26
<211> 30
<212> PRT

<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-methylhistidine

<210>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
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<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 26
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 27
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-methylhistidine

<210>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<210>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 27
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg

20 25 30

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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg

20 25 30

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<400> 32
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1 5 10 15
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20 25 30

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1 5 10 15
Gln Xaa Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg

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1 5 10 15
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
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<210> 37
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<400> 37
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Gln Ala Ala Lys Glu Phe Xaa Ala Trp Xaa Val Lys Xaa Arg
             20   25   30

<210> 38
<211> 30
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 39
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 40
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1 5 10 15
Gln Ala Lys Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
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<210> 41
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1 5 10 15
Gln Xaa Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 42
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<220>
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<400> 42
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Xaa Ala Trp Xaa Val Lys Xaa Arg
             20   25   30

<210> 43
<211> 30
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<223> this sequence has an amidated c-terminus

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1 5 10 15
Gln Xaa Ala Lys Glu Phe Xaa Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 44
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 45
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 46
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<221> MOD_RES
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<220>
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Xaa Lys Xaa Arg
20 25 30

<210> 47
<211> 30
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<220>
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 48
<211> 30
<212> PRT
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<220>
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<220>
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<220>
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<400> 48
His Xaa Glu Gly Thr Phe Thr Ser Asp Xaa Ser Ser Tyr Xaa Glu Gly

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  1               5                  10                  15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20                  25                  30

<210> 49
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<212> PRT
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<400> 49
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Xaa
  1               5                  10                  15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20                  25                  30

<210> 50
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<400> 50
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 51
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<212> PRT
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<223> alpha-aminoisobutyric acid

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<400> 51
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1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 52
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<220>
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<400> 52
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  1   5   10   15
Glu Xaa Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
             20   25   30

<210> 53
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<220>
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<220>
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<223> this sequence has an amidated c-terminus

<400> 53

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Xaa Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 54
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<220>
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<400> 54
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1 5 10 15
Glu Xaa Xaa Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 55

<211> 30
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<220>
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<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 55
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  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
             20   25   30

<210> 56
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<220>
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<221> MOD_RES
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<223> this sequence has an amidated c-terminus

<400> 56

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His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1               5                  10                  15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
             20                  25                  30

<210> 57
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<220>
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<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 57
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1               5                  10                  15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20                  25                  30

<210> 58
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<212> PRT
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<220>
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<220>
<223> this sequence has an amidated c-terminus
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<400> 58
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1 5 10 15
Gln Xaa Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 59
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<400> 59
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1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Xaa Trp Leu Val Lys Xaa Arg
20 25 30

<210> 60
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<220>
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<400> 60
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Xaa Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 61
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<220>
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<220>
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<220>
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<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 61
His Xaa Glu Gly Thr Phe Thr Ser Asp Xaa Ser Ser Tyr Xaa Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 62
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (10)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (23)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 62
His Xaa Glu Gly Thr Phe Thr Ser Asp Xaa Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Xaa Ala Trp Xaa Val Lys Xaa Arg
             20   25   30

<210> 63
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 63
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Xaa Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 64
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 64
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Xaa Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 65
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)

<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 65
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 66
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (14)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 66
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Xaa Glu Gly
1 5 10 15
Gln Xaa Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 67
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 67
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Xaa Ala Trp Xaa Val Lys Xaa Arg
             20   25   30

<210> 68
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (23)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 68
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Xaa Ala Lys Glu Phe Xaa Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 69
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 69
His Xaa Glu Gly Thr Xaa Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 70
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (14)

<223> cyclohexylalanine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 70
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Xaa Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 71
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 71
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Xaa Lys Xaa Arg
20 25 30

<210> 72
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 72
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Xaa Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 73
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

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<223> beta-alanine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 73
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Xaa
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 74
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 74
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Xaa
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 75
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 75
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 76
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

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<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 76
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 77
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 77
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Glu Xaa Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
             20   25   30

<210> 78
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<220>
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<223> alpha-aminoisobutyric acid

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<223> alpha-aminoisobutyric acid

<220>
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 78
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Xaa Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
20 25 30

<210> 79
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

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<223> 1-amino-1-cyclohexanecarboxylic acid

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<223> 1-amino-1-cyclohexanecarboxylic acid

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<223> alpha-aminoisobutyric acid

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<223> alpha-aminoisobutyric acid

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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 79
His Xaa Glu Gly Thr Phe Thr Ser Asp Xaa Ser Ser Tyr Xaa Glu Gly

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  1               5                  10                  15
Glu Xaa Xaa Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Arg
             20                  25                  30

<210> 80
<211> 30
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<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 80
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1               5                  10                  15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20                  25                  30

<210> 81
<211> 30
<212> PRT
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<220>
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<220>
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<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 81
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1               5                  10                  15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20                  25                  30
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<210> 82
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 82
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 83
<211> 30
<212> PRT
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<220>
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<223> beta-alanine

<220>
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<400> 83
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 84
<211> 30
<212> PRT
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<220>
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<223> beta-alanine

<220>
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<400> 84
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 85
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<220>
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<220>
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<400> 85
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa Gly
20 25 30

<210> 86
<211> 31
<212> PRT
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<220>
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<220>
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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
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<223> alpha-aminoisobutyric acid

<400> 86
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa Xaa
             20   25   30

<210> 87
<211> 32
<212> PRT
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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<400> 87
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 88
<211> 32
<212> PRT
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<220>
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<223> beta-alanine

<220>
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<400> 88
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 89
<211> 32
<212> PRT
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<400> 89
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1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 90
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (31)
<223> beta-alanine

<400> 90
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Gly Xaa Xaa
20 25 30

<210> 91
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<220>
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<400> 91
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Gly Xaa Xaa
20 25 30

<210> 92
<211> 31
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<220>
<221> MOD_RES
<222> (31)
<223> 12-aminododecanoic acid

<400> 92
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa
20 25 30

<210> 93
<211> 31
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<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<220>
<221> MOD_RES
<222> (31)
<223> 12-aminododecanoic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 93
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa
20 25 30

<210> 94
<211> 32
<212> PRT
<213> Artificial Sequence

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<220>
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<220>
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<222> (32)
<223> N-epsilon-tetradecanoyl-lysine

<400> 94
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Gly Arg Xaa Xaa
20 25 30

<210> 95
<211> 32
<212> PRT
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<220>
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<220>
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<223> beta-alanine

<220>
<221> MOD_RES
<222> (32)
<223> N-epsilon-tetradecanoyl-lysine

<400> 95
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Gly Arg Xaa Xaa
20 25 30

<210> 96
<211> 32
<212> PRT
<213> Artificial Sequence

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<220>
<221> MOD_RES
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<223> N-epsilon-octanoyl-lysine

<220>
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<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 96
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Gly Arg Xaa Xaa
20 25 30

<210> 97
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 97
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 98
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 98
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 99
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 99
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 100
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 100
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 101

<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (20)
<223> N-epsilon-hexaxecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 101
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 102
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 102

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 103
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 103
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 104
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (20)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 104
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 105
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (20)
<223> N-epsilon-decanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 105
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 106
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (20)

<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 106
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Lys Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

<210> 107
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (20)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 107
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Lys Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

<210> 108
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<220>
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<222> (20)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 108
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 109
<211> 30
<212> PRT
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<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (20)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 109
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 110
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 110
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 111
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 111
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 112
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-decanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 112
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 113
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 113
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 114
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 114
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 115
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)

<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 115
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 116
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-decanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 116
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 117
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 117
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 118
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 118
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 119
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 119
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 120
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 120
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 121
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 121
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 122
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-decanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 122
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 123
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 123
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 124
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 124
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 125
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 125
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 126
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-decanoyl-lysine

<220>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 126
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 127
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 127
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 128
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 128
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 129
<211> 30
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 129
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 130
<211> 30
<212> PRT
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<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 130
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 131
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 131
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 132
<211> 30
<212> PRT
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<220>

<223> Mutagen

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<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 132
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 133
<211> 30
<212> PRT
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<220>
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<220>
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<223> N-epsilon-octanoyl-lysine

<220>
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<400> 133
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1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 134
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<212> PRT
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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 134
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 135
<211> 30
<212> PRT
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<220>
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<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 135
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 136
<211> 30
<212> PRT
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<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 136
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 137
<211> 30
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<221> MOD_RES
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 137
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 138
<211> 32
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<221> MOD_RES
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<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 138
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 139
<211> 32
<212> PRT
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<220>
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<223> N-epsilon-decanoyl-lysine

<220>
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<400> 139
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 140
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<220>
<221> MOD_RES
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 140
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 141
<211> 32
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 141
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

<210> 142
<211> 32
<212> PRT
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<220>
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<222> (32)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 142
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly

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  1               5                  10                  15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20                  25                  30

<210> 143
<211> 32
<212> PRT
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<220>
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<223> N-epsilon-decanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 143
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1               5                  10                  15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20                  25                  30

<210> 144
<211> 32
<212> PRT
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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 144
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 145
<211> 32
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<220>
<223> this sequence has an amidated c-terminus

<400> 145
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

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<211> 32
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<222> (32)
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<220>
<223> this sequence has an amidated c-terminus

<400> 146
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30

<210> 147
<211> 32
<212> PRT
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<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 147
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 148
<211> 32
<212> PRT
<213> Artificial Sequence

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<220>
<223> this sequence has an amidated c-terminus

<400> 148
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 149
<211> 32
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<220>
<223> this sequence has an amidated c-terminus

<400> 149
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30

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<223> N-epsilon-decanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 150
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 151
<211> 32
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<221> MOD_RES
<222> (32)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 151
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 152
<211> 32
<212> PRT
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<223> alpha-aminoisobutyric acid

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<223> alpha-aminoisobutyric acid

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<221> MOD_RES
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 152
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 153
<211> 30
<212> PRT
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<223> N-epsilon-octanoyl-lysine

<220>
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<400> 153
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 154
<211> 30
<212> PRT
<213> Artificial Sequence

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<221> MOD_RES
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 154
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 155
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 155
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 156
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<212> PRT
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<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 156
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 157
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 157
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

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<220>
<223> this sequence has an amidated c-terminus

<400> 158
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 159
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His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 160
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<220>
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<220>
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<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 160
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 161
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<212> PRT
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<220>
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<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 161
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 162
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<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 162
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 163
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<220>
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<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 163
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

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<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 164

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 165
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<220>
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<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 165
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

<210> 166
<211> 30
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<220>
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<223> N-epsilon-octanoyl-lysine

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<221> MOD_RES
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<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 166
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 167
<211> 30
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<220>
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<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 167
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 168
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 168
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 169
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-decanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 169
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 170
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 170
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 171
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 171
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 172
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (28)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 172
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 173
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> N-epsilon-decanoyl-lysine

<220>
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<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 173
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 174
<211> 30
<212> PRT
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<220>
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<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 174
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 175
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)

<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 175
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 176
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 176
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 177
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> beta-alanine

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<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 177
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
             20   25   30

<210> 178
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> beta-alanine

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 178
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
             20   25   30

<210> 179
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

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<222> (29)
<223> beta-alanine

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 179
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 180
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> beta-alanine

<220>
<221> MOD_RES
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<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 180
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 181
<211> 30
<212> PRT
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<220>

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<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 181
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 182
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 182
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 183
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<222> (29)
<223> beta-alanine

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<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 183
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 184
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> beta-alanine

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<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 184
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 185
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (29)
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<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 185
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 186
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<220>
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<222> (30)

<223> N-epsilon-decanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 186
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 187
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> beta-alanine

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 187
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 188
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 188
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 189
<211> 30
<212> PRT
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 189
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Lys Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 190
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
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<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 190
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 191
<211> 30
<212> PRT
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<220>
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<223> beta-alanine

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 191
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 192
<211> 30
<212> PRT
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<220>

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<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 192
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 193
<211> 30
<212> PRT
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<223> beta-alanine

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-decanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 193
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 194
<211> 30
<212> PRT
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<220>
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<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cylohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 194
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Xaa Val Arg Xaa Arg
             20   25   30

<210> 195
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
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<223> 1-amino-1-cylohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 195
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Xaa Val Arg Xaa Arg
20 25 30

<210> 196
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<223> alpha-aminoisobutyric acid

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<222> (20)
<223> N-epsilon-hexadecanoyl-lysine

<220>
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<222> (26)
<223> 1-amino-1-cylohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 196
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Xaa Val Arg Xaa Arg
20 25 30

<210> 197
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<212> PRT
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<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 197
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
             20   25   30

<210> 198
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> 1-amino-1-cylohexanecarboxylic acid

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 198
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

<210> 199
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> alpha-aminoisobutyric acid

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<223> 1-amino-1-cylohexanecarboxylic acid

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<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 199
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

<210> 200
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cylohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 200
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
             20   25   30

<210> 201
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<212> PRT
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<220>
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<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 201

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

<210> 202
<211> 30
<212> PRT
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<220>
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<223> alpha-aminoisobutyric acid

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<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 202
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 203
<211> 30
<212> PRT
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<220>
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<223> 1-amino-1-cylohexanecarboxylic acid

<220>
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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 203
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 204
<211> 30
<212> PRT
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<220>
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 204
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 205
<211> 30
<212> PRT
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<220>
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<220>
<221> MOD_RES
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<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 205
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
             20   25   30

<210> 206
<211> 30
<212> PRT
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 206
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 207
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<212> PRT
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 207
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 208
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<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 208
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
             20   25   30

<210> 209
<211> 30
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<220>
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<222> (30)
<223> N-epsilon-decanoyl-lysine

<220>
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<400> 209
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 210
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<212> PRT
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<220>
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<220>
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<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 210
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 211
<211> 30
<212> PRT
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 211
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
             20   25   30

<210> 212
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 212

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Xaa Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 213
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 213
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Xaa Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 214
<211> 30
<212> PRT
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<220>
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<400> 214
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Xaa Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 215
<211> 30
<212> PRT
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<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 215
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Xaa Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 216
<211> 30
<212> PRT
<213> Artificial Sequence

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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 216
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Xaa Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
             20   25   30

<210> 217
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<212> PRT
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<223> N-epsilon-hexadecanoyl-lysine

<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 217
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Xaa Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
             20   25   30

<210> 218
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 218
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Xaa Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
             20   25   30

<210> 219
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<220>

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<220>
<223> this sequence has an amidated c-terminus

<400> 219
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Xaa Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
             20   25   30

<210> 220
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 220
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Xaa Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 221
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<220>
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 221
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

<210> 222
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<220>

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<220>
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<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 222
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 223
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<212> PRT
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<220>
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<220>
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<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 223
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 224
<211> 30
<212> PRT
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<220>
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<223> N-epsilon-hexadecanoyl-lysine

<220>
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<220>
<223> this sequence has an amidated c-terminus

<400> 224
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 225
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<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> N-epsilon-octanoyl-lysine

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<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
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<400> 225
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 226
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<212> PRT
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<220>
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<223> 1-amino-1-cylohexanecarboxylic acid

<220>
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<223> N-epsilon-octanoyl-lysine

<220>
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<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 226
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Xaa Xaa Arg
20 25 30

<210> 227
<211> 30
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<220>
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<223> N-epsilon-octanoyl-lysine

<220>
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<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 227
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 228
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 228
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 229
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<220>
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<220>
<221> MOD_RES
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<220>
<223> this sequence has an amidated c-terminus

<400> 229
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 230
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 230
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 231
<211> 30
<212> PRT
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<220>

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<223> N-epsilon-tetradecanoyl-lysine

<220>
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<400> 231
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 232
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<212> PRT
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<220>
<221> MOD_RES
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 232
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Xaa
20 25 30

<210> 233
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<220>
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<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 233
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 234
<211> 30
<212> PRT
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<220>
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<220>
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<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 234
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 235
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 235
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 236
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (24)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 236
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Xaa Trp Leu Val Arg Xaa Arg
20 25 30

<210> 237
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 237
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Xaa Trp Leu Val Arg Xaa Arg
20 25 30

<210> 238
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 238
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Xaa Glu Phe Ile Xaa Trp Leu Val Arg Xaa Arg
             20   25   30

<210> 239
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-octanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 239
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Xaa Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 240
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 240
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Xaa Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 241
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
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<222> (28)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 241
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Xaa Trp Leu Val Xaa Xaa Arg
             20   25   30

<210> 242
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
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<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 242

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Xaa Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 243
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (24)
<223> alpha-aminoisobutyric acid

<220>
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<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 243
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Xaa Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 244
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 244
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Xaa Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 245
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 245
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 246
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 246
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
             20   25   30

<210> 247
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 247
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Lys Glu Phe Ile Ala Trp Xaa Val Lys Xaa Xaa
20 25 30

<210> 248
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
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<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 248
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 249
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 249
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
             20   25   30

<210> 250
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 250
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Ala Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 251
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 251
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 252
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 252
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Glu Xaa Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
             20   25   30

<210> 253
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 253
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Glu Xaa Ala Arg Glu Phe Ile Ala Trp Xaa Val Arg Xaa Xaa
             20   25   30

<210> 254
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-octanoyl-lysine

<220>

<223> this sequence has an amidated c-terminus

<400> 254
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Ala Arg Glu Phe Ile Xaa Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 255
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-tetradecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 255
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Glu Xaa Ala Arg Glu Phe Ile Xaa Trp Xaa Val Arg Xaa Xaa
20 25 30

<210> 256
<211> 30
<212> PRT

<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (18)
<223> alpha-aminoisobutyric acid

<220>
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<222> (24)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (26)
<223> 1-amino-1-cyclohexanecarboxylic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanoyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 256
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Glu Xaa Ala Arg Glu Phe Ile Xaa Trp Xaa Val Arg Xaa Xaa
             20   25   30

<210> 257
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazine-ethanesulfonyl)-
      histidine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 257
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 258
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazine-ethanesulfonyl)-
histidine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 258
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 259
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazine-ethanesulfonyl)-
histidine

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 259
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 260
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazineacetyl)-
histidine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 260
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 261
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazineacetyl)-
histidine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 261
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 262
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-(4-(2-hydroxyethyl)-1-piperazineacetyl)-
histidine

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 262
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 263
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)

<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 263
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 264
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 264
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
             20   25   30

<210> 265
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 265
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 266
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 266
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa Arg
20 25 30

<210> 267
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)

<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 267
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 268
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 268
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 269
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 269
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 270
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 270
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 271
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)

<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 271
Xaa Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 272
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)
<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 272
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 273
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (1)

<223> N-alpha-tetradecanoyl-histidine

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> beta-alanine

<220>
<223> this sequence has an amidated c-terminus

<400> 273
Xaa Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 274
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-octanesulfonyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 274
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 275
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-dodecanesulfonyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 275
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 276
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-hexadecanesulfonyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 276
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 277
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-octanesulfonyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 277
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 278
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-dodecanesulfonyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 278
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 279
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-hexadecanesulfonyl-lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 279
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 280
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)

<223> N-epsilon-octanesulfonyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 280
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 281
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-hexadecanesulfonyl-lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 281
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 282
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)

<223> (1-(4-decylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 282
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 283
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 283
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 284
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 284
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

<210> 285
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 285
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

<210> 286
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 286
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 287
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 287
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 288
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 288
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 289
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 289
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 290
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 290
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 291
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)

<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 291
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 292
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 292
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 293
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 293
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

<210> 294
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 294
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

<210> 295
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 295
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 296
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 296
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 297
<211> 32
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 297
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30

<210> 298
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 298
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 299
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 299
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 300
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 300
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 301
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 301
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 302
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 302
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 303
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 303
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 304
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 304
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 305
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> (1-(4-decylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 305
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 306
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 306
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 307
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)

<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 307
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 308
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 308
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 309
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 309
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 310
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 310
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 311
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 311
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 312
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 312
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 313
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 313
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 314
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
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<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 314
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 315
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 315
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 316
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)

<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 316
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 317
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-decylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 317
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 318
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-dodecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 318
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30

<210> 319
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
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<223> alpha-aminoisobutyric acid

<220>
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<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-tetradecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 319

His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 320
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
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<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-(4-hexadecylpiperazine))aspartic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 320
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 321
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> (1-dodecylamino))glutamic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 321
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 322
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> (1-dodecylamino))glutamic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 322
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 323
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> (1-dodecylamino))glutamic acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 323
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 324
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (31)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> (1-dodecylamino))glutamic acid

<220>
<223> this sequence has an amidated c-terminus

<400> 324
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 325
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-(2-(4-decyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 325
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

<210> 326
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-(2-(4-dodecyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 326
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 327
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-(2-(4-tetradecyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 327
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 328
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (20)
<223> N-epsilon-(2-4-hexadecyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)

<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 328
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

<210> 329
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
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<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-(2-(4-decyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 329
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 330
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)

<223> N-epsilon-(2-(4-dodecyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 330
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 331
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-(2-(4-tetradecyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 331
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 332
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)

<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (28)
<223> N-epsilon-(2-(4-hexadecyl-1-piperazine)-acetyl)lysine

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<223> this sequence has an amidated c-terminus

<400> 332
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 333
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-(2-(4-decyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 333
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 334
<211> 30
<212> PRT
<213> Artificial Sequence

<220>

<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-(2-(4-dodecyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 334
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 335
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (30)
<223> N-epsilon-(2-(4-hexadecyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 335
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 336
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> N-epsilon-(2-(4-decyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 336
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

<210> 337
<211> 32
<212> PRT
<213> Artificial Sequence

<220>
<223> Mutagen

<220>
<221> MOD_RES
<222> (2)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (29)
<223> alpha-aminoisobutyric acid

<220>
<221> MOD_RES
<222> (32)
<223> N-epsilon-(2-(4-dodecyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 337
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
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20 25 30

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<211> 32
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<220>
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<400> 338
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1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
20 25 30

<210> 339
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<223> N-epsilon-(2-(4-hexadecyl-1-piperazine)-acetyl)lysine

<220>
<223> this sequence has an amidated c-terminus

<400> 339
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1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
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<400> 340
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1 5 10 15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 341
<211> 32
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Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30

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<400> 342

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His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
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Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20                  25                  30

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<400> 343
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  1               5                  10                  15
Gln Ala Ala Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20                  25                  30

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  1   5   10   15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

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<400> 345
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
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Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
             20   25   30

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<400> 346
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Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

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His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Xaa Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg
20 25 30

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<400> 348
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  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
             20   25   30

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<400> 349
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
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             20   25   30

<210> 350
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Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

<210> 351
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<212> PRT
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<400> 351
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Xaa Xaa Arg
20 25 30

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<400> 352
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1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

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<400> 353
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1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 354
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<400> 354
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1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
20 25 30

<210> 355
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  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Xaa
             20   25   30

<210> 356
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<212> PRT
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<400> 356
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

<210> 357
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<400> 357
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

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<400> 358
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
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Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

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<400> 359
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Gly Xaa
             20   25   30

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<400> 360

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1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 361
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<220>
<223> this sequence has an amidated c-terminus

<400> 361
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1 5 10 15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
20 25 30

<210> 362
<211> 32
<212> PRT
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<220>
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<400> 362
His Xaa Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30

<210> 363
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<400> 363
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  1   5   10   15
Gln Ala Arg Arg Glu Phe Ile Ala Trp Leu Val Arg Xaa Arg Xaa Xaa
             20   25   30