

SEQUENCE LISTING

<110> Eli Lilly and Company

<120> INCRETIN ANALOGS AND USES THEREOF

<130> X21606

<150> US 62/608,613

<151> 2017-12-21

<160> 27

<170> PatentIn version 3.5

<210> 1

<211> 29

<212> PRT

<213> Homo sapiens

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His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser
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Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Met	Asn	Thr
			20					25				

<210> 2

<211> 30

<212> PRT

<213> Homo sapiens

<400> 2

His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Val	Ser	Ser	Tyr	Leu	Glu	Gly
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Gln	Ala	Ala	Lys	Glu	Phe	Ile	Ala	Trp	Leu	Val	Lys	Gly	Arg
			20					25					30

<210> 3

<211> 37

<212> PRT

<213> Homo sapiens

<400> 3

His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser
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Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Lys Arg Asn
20 25 30

Arg Asn Asn Ile Ala
35

<210> 4
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<213> Homo sapiens

<400> 4

Tyr Ala Glu Gly Thr Phe Ile Ser Asp Tyr Ser Ile Ala Met Asp Lys
1 5 10 15

Ile His Gln Gln Asp Phe Val Asn Trp Leu Leu Ala Gln Lys Gly Lys
20 25 30

Lys Asn Asp Trp Lys His Asn Ile Thr Gln
35 40

<210> 5
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<220>
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<220>
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<222> (2)..(2)
<223> Xaa at position 2 is Aib

<220>
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<222> (13)..(13)
<223> Xaa at position 13 is Leu or alpha-methyl-Leu

<220>
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<222> (17)..(17)
<223> Xaa at position 17 is any amino acid with a functional group
available for conjugation wherein the functional group is
conjugated to a C16-C22 fatty acid

<220>
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 <223> Xaa at position 19 is Gln or Ala

<220>
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 <223> Xaa at position 20 is Aib, alpha-methyl-Lys, Gln, or His

<220>
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 <222> (28)..(28)
 <223> Xaa at position 28 is Glu or Ala

<220>
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 <222> (29)..(29)
 <223> Xaa at position 29 is Gly or Aib

<220>
 <221> MISC_FEATURE
 <222> (34)..(34)
 <223> Xaa at position 34 is Gly or Aib

<400> 5

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
 1 5 10 15

Xaa Ala Xaa Xaa Ala Phe Ile Glu Tyr Leu Leu Xaa Xaa Gly Pro Ser
 20 25 30

Ser Xaa Ala Pro Pro Pro Ser
 35

<210> 6
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 <223> Xaa at position 2 is alpha-amino-isobutyric acid

<220>
 <221> MISC_FEATURE
 <222> (13)..(13)
 <223> Xaa at position 13 is alpha-methyl-Leu

 <220>
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 <222> (17)..(17)
 <223> Lys at position 17 is modified with
 (2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH2)18-HCO
 2H

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 <222> (29)..(29)
 <223> Xaa at position 29 is alpha-amino-isobutyric acid

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 <222> (39)..(39)
 <223> Ser at position 39 is optionally amidated

 <400> 6

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
 1 5 10 15

Lys Ala Gln His Ala Phe Ile Glu Tyr Leu Leu Ala Xaa Gly Pro Ser
 20 25 30

Ser Gly Ala Pro Pro Pro Ser
 35

<210> 7
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 <223> Xaa at position 2 is alpha-amino-isobutyric acid

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 <222> (13)..(13)
 <223> Xaa at position 13 is alpha-methyl-Leu

<220>
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 <222> (17)..(17)
 <223> Lys at position 17 is chemically modified by conjugation of the
 epsilon-amino group of the Lys side chain with
 (2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
 2H)

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 <223> Xaa at position 20 is alpha-methyl-Lys

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 <222> (29)..(29)
 <223> Xaa at position 29 is alpha-amino-isobutyric acid

<220>
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 <222> (39)..(39)
 <223> Ser at position 39 is optionally amidated

<400> 7

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
 1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Ala Xaa Gly Pro Ser
 20 25 30

Ser Gly Ala Pro Pro Pro Ser
 35

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<222> (13)..(13)
 <223> Xaa at position 13 is alpha-methyl-Leu

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 <223> Lys at position 17 is chemically modified by conjugation of the
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 2H)

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 <223> Xaa at position 20 is alpha-methyl-Lys

<220>
 <221> MOD_RES
 <222> (39)..(39)
 <223> Ser at position 39 is optionally amidated

<400> 8

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
 1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
 20 25 30

Ser Gly Ala Pro Pro Pro Ser
 35

<210> 9
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 <223> Lys at position 17 is chemically modified by conjugation of the
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(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH₂)₁₈-CO₂H

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<222> (20)..(20)

<223> Xaa at position 20 is alpha-amino-isobutyric acid

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<222> (29)..(29)

<223> Xaa at position 29 is alpha-amino-isobutyric acid

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<221> MOD_RES

<222> (39)..(39)

<223> Ser at position 39 is optionally amidated

<400> 9

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Leu Leu Asp Lys
1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Ala Xaa Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<223> Xaa at position 13 is alpha-methyl-Leu

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<223> Lys at position 17 is chemically modified by conjugation of the epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
2H

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<222> (29)..(29)

<223> Xaa at position 29 is alpha-amino-isobutyric acid

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<400> 10

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Xaa	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Ala	Gln	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
						35

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<222> (13)..(13)

<223> Xaa at position 13 is alpha-methyl-Leu

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<221> MOD_RES

<222> (17)..(17)

<223> Lys at position 17 is chemically modified by conjugation of the epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO

2H

<220>

<221> MOD_RES

<222> (39)..(39)

<223> Ser at position 39 is optionally amidated

<400> 11

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
1 5 10 15

Lys Ala Ala Gln Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 12

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<222> (2)..(2)

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<222> (13)..(13)

<223> Xaa at position 13 is alpha-methyl-Leu

<220>

<221> MOD_RES

<222> (17)..(17)

<223> Lys at position 17 is chemically modified by conjugation of the
epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
2H

<220>

<221> MOD_RES

<222> (39)..(39)

<223> Ser at position 39 is optionally amidated

<400> 12

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
1 5 10 15

Lys Ala Gln His Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<223> Xaa at position 2 is alpha-amino-isobutyric acid

<220>
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<222> (17)..(17)
<223> Lys at position 17 is chemically modified by conjugation of the
epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
2H

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<223> Xaa at position 20 is alpha-methyl-Lys

<220>
<221> MOD_RES
<222> (39)..(39)
<223> Ser at position 39 is optionally amidated

<400> 13

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Leu Leu Asp Lys
1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<223> Xaa at position 2 is alpha-amino-isobutyric acid

<220>
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<223> Xaa at position 13 is alpha-methyl-Leu

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<222> (17)..(17)
<223> Lys at position 17 is chemically modified by conjugation of the
epsilon-amino group of the Lys side chain with
(gamma-Glu)2-CO-(CH2)18-CO2H

<220>
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<222> (39)..(39)
<223> Ser at position 39 is optionally amidated

<400> 14

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Xaa Leu Asp Lys
1 5 10 15

Lys Ala Gln His Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 15
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<220>
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<223> Xaa at position 2 is alpha-amino-isobutyric acid

<220>
<221> MISC_FEATURE
<222> (13)..(13)
<223> Xaa at position 13 is alpha-methyl-Leu

<220>
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<222> (17)..(17)
<223> Lys at position 17 is chemically modified by conjugation of the
epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH₂)₁₈-CO₂
H

<220>
<221> MOD_RES
<222> (39)..(39)
<223> Ser at position 39 is optionally amidated

<400> 15

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Xaa	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Gln	His	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Gly	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

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<223> Synthetic Construct

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<223> Xaa at position 2 is alpha-amino-isobutyric acid

<220>

<221> MISC_FEATURE

<222> (13)..(13)

<223> Xaa at position 13 is alpha-methyl-Leu

<220>

<221> MOD_RES

<222> (17)..(17)

<223> Lys at position 17 is chemically modified by conjugation of the epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
2H

<220>

<221> MISC_FEATURE

<222> (20)..(20)

<223> Xaa at position 20 is alpha-amino-isobutyric acid

<220>

<221> MOD_RES

<222> (39)..(39)

<223> Ser at position 39 is optionally amidated

<400> 16

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Xaa	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Gln	Xaa	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Gly	Gly	Pro	Ser
		20					25					30			

Ser	Gly	Ala	Pro	Pro	Pro	Ser
		35				

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<223> Synthetic Construct

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 <223> Lys at position 17 is chemically modified by conjugation of the
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 H

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 <223> Xaa at position 20 is alpha-amino-isobutyric acid

<220>
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 <222> (39)..(39)
 <223> Ser at position 39 is optionally amidated

<400> 17

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Xaa	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Gln	Xaa	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Gly	Gly	Pro	Ser
		20						25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
		35				

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<220>
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 <222> (13)..(13)
 <223> Xaa at position 13 is alpha-methyl-Leu

<220>
 <221> MOD_RES
 <222> (17)..(17)
 <223> Lys at position 17 is chemically modified by conjugation of the
 epsilon-amino group of the Lys side chain with
 (2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH2)18-CO2
 H

<220>
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 <223> Xaa at position 20 is alpha-amino-isobutyric acid

<220>
 <221> MISC_FEATURE
 <222> (29)..(29)
 <223> Xaa at position 29 is alpha-amino-isobutyric acid

<220>
 <221> MOD_RES
 <222> (39)..(39)
 <223> Ser at position 39 is optionally amidated

<400> 18

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Xaa	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Gln	Xaa	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Xaa	Gly	Pro	Ser
		20					25						30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
		35				

<210> 19
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<222> (13)..(13)
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 <222> (17)..(17)
 <223> Lys at position 17 is chemically modified by conjugation of the
 epsilon-amino group of the Lys side chain with
 (2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH2)18-CO2H

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 <223> Xaa at position 20 is alpha-amino-isobutyric acid

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<220>
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 <222> (34)..(34)
 <223> Xaa at position 34 is alpha-amino-isobutyric acid

<220>
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 <222> (39)..(39)
 <223> Ser at position 39 is optionally amidated

<400> 19

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Xaa	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Gln	Xaa	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Xaa	Gly	Pro	Ser
		20					25						30		

Ser	Xaa	Ala	Pro	Pro	Pro	Ser
		35				

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 <223> Lys at position 17 is chemically modified by conjugation of the
 epsilon-amino group of the Lys side chain with
 (2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
 2H

<220>
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 <223> Xaa at position 20 is alpha-amino-isobutyric acid

<220>
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<220>
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<400> 20

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Leu	Leu	Asp	Lys
1				5					10					15	

Lys	Ala	Gln	Xaa	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Ala	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
			35			

<210> 21
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<220>
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<223> Lys at position 17 is chemically modified by conjugation of the
epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
2H

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<220>
<221> MOD_RES
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<400> 21

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Leu Leu Asp Lys
1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)2-(gamma-Glu)-CO-(CH2)18-CO
2H

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<220>
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<223> Xaa at position 29 is alpha-amino-isobutyric acid

<220>
<221> MOD_RES
<222> (39)..(39)
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<400> 22

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Leu Leu Asp Lys
1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Glu Xaa Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 23
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epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH2)18-CO2
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<222> (20)..(20)
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<220>
<221> MOD_RES
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<223> Ser at position 39 is optionally amidated

<400> 23

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Leu Leu Asp Lys
1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Glu Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 24
<211> 39
<212> PRT
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<220>
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<220>
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<222> (2)..(2)
<223> Xaa at position 2 is alpha-amino-isobutyric acid

<220>
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<222> (17)..(17)
<223> Lys at position 17 is chemically modified by conjugation of the
epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)2-CO-(CH2)18-CO
2H

<220>
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<222> (20)..(20)
<223> Xaa at position 20 is alpha-amino-isobutyric acid

<220>
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<222> (29)..(29)
<223> Xaa at position 29 is alpha-amino-isobutyric acid

<220>
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<222> (39)..(39)
<223> Ser at position 39 is optionally amidated

<400> 24

Tyr Xaa Gln Gly Thr Phe Thr Ser Asp Tyr Ser Ile Leu Leu Asp Lys
1 5 10 15

Lys Ala Gln Xaa Ala Phe Ile Glu Tyr Leu Leu Glu Xaa Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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epsilon-amino group of the Lys side chain with
(2-[2-(2-Amino-ethoxy)-ethoxy]-acetyl)-(gamma-Glu)-CO-(CH₂)₁₈-CO₂
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<223> Ser at position 39 is optionally amidated

<400> 25

Tyr	Xaa	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Ile	Leu	Leu	Asp	Lys
1				5				10						15	

Lys	Ala	Gln	Xaa	Ala	Phe	Ile	Glu	Tyr	Leu	Leu	Glu	Xaa	Gly	Pro	Ser
			20					25					30		

Ser	Gly	Ala	Pro	Pro	Pro	Ser
						35

<210> 26

<211> 10

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<220>

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<400> 26

Gly	Pro	Ser	Ser	Gly	Ala	Pro	Pro	Pro	Ser
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<210> 27

<211> 10

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<223> Synthetic Construct

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<222> (5)..(5)

<223> Xaa at position 5 is alpha-amino-isobutyric acid

<400> 27

Gly	Pro	Ser	Ser	Xaa	Ala	Pro	Pro	Pro	Ser
1				5					10