

MOLECULES AND METHODS OF USE THEREOF**CROSS-REFERENCE TO RELATED APPLICATIONS**

This application claims the benefit of priority of U.S. Provisional patent application no. 63/498,511 filed on April 26, 2023, the content of which is hereby incorporated by reference in
5 its entirety.

SEQUENCE LISTING

The instant application contains a sequence listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on April 19, 2024, is named Woolwich_001_WO1_SL, and is 2,453,732 bytes in size.

10 INCORPORATION-BY-REFERENCE

For the purposes of only those jurisdictions that permit incorporation by reference, the content of all documents cited herein is hereby incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

Opioid receptors are 7-transmembrane G-protein coupled receptors. The four types of opioid
15 receptors are termed mu, delta, kappa, and nociceptin receptors. Endogenous opioids and opioid drugs activate these opioid receptors and can produce analgesic effects as well as other biological effects. Studies suggest that delta opioid receptor agonists may have a role in a variety of therapeutic areas including but not limited to chronic and acute pain management¹⁻²⁵.

However, although several delta opioid agonists have been identified, none have yet been
20 approved by a regulatory body for the treatment of pain or any other condition. For at least the following reasons, there is a need in the art for new agonists of delta opioid receptors:

- First, there is a need for chemically novel delta opioid agonists to facilitate the mechanistic understanding of the delta opioid receptor's role in human pathophysiology.
- Second, there is a need for chemically novel delta opioid agonists that are safe and avoid
25 some of the adverse events (such as convulsions) that have been observed with prior delta opioid agonists.
- Third, there is a need for chemically novel molecules including chemically novel delta opioid agonists that exhibit clinical analgesic efficacy.
- Fourth, there is a need for chemically novel molecules including chemically novel delta
30 opioid agonists that have a sufficiently long duration of action to make them clinically useful (such as for the treatment of pain).

- Fifth, there is a need for chemically novel molecules including chemically novel delta opioid agonists that are effective (such as for the treatment of pain) when delivered orally.
- Sixth, there is a need for chemically novel molecules including chemically novel delta opioid agonists that exhibit analgesic efficacy in a range of animal species including in non-human
5 primates.
- Seventh, there is a need for chemically novel molecules including chemically novel delta opioid agonists that exhibit analgesic efficacy in a range of animal models such as acute mechanical pain, acute thermal pain, inflammatory pain, visceral pain, and/or neuropathic pain.
- 10 • Eighth, there is a need for chemically novel analgesic molecules including chemically novel delta opioid agonists that have a site of action not in the central nervous system.
- Ninth, there is a need for chemically novel analgesic molecules including chemically novel delta opioid agonists that do not exhibit any undesirable neurological effects such as narcotic effects.
- 15 • Tenth, there is a need for chemically novel analgesic molecules including chemically novel delta opioid agonists that do not induce tolerance upon repeated administration and can maintain clinical efficacy over repeated administrations.
- Eleventh, there is a need for chemically novel delta opioid agonists that have analgesic efficacy predominantly mediated by the delta opioid receptor and not the mu opioid receptor
20 (for example as demonstrated through use of antagonists and/or genetic knock-out models).
- Twelfth, there is a need for chemically novel delta opioid agonists that are stable for extended periods of time as a solid and/or in solution at room temperature and/or at elevated temperatures.
- Thirteenth, there is a need for chemically novel delta opioid agonists that are stable in acidic
25 and/or peroxidic solutions, and/or under ultraviolet light.
- Fourteenth, there is a need for chemically novel delta opioid agonists that are biased DOR agonists, for example having a higher potency (lower EC₅₀) and/or activity (higher maximal effect) for one downstream effect of DOR agonism (such as cAMP production or calcium flux) over another (such as beta arrestin recruitment or receptor internalization).
- 30 The present invention aims to address these needs.

SUMMARY OF THE INVENTION

The present invention is based, in part, on a series of important developments and discoveries relating to delta opioid receptor agonists, further details of which are provided in the “Examples”

and “Detailed Description of the Invention” sections of this patent disclosure. In brief, a panel of novel peptides have been developed that have delta opioid receptor agonist activity and that are chemically novel, do not demonstrate convulsions in animals, exhibit analgesic efficacy in animal models, maintain analgesic efficacy for clinically useful durations in animal models, and/or are effective at exhibiting analgesic efficacy when administered orally. Building on these developments, the present invention provides a variety of new peptide agonists of delta opioid receptors, compositions comprising such peptides, and methods of use of such peptides.

Several of the peptides of the present invention are identified herein using sequence identification number (SEQ ID NO:) and/or a peptide number (PEP NO:). Peptides that meet the requirements for inclusion in a sequence listing are assigned both a PEP NO: and a SEQ ID NO: of the same number. Peptides that have amino acid sequences that do not meet the requirements for inclusion in a sequence listing (i.e., peptides having fewer than 4 defined amino acids) are assigned only a PEP NO:), as further described in the “Definitions & Abbreviations” section of this patent disclosure. The phrase “SEQ ID NO: and/or PEP NO:” (or the plural form “SEQ ID NOs: and/or PEP NOs:”) and “PEP NO: and/or SEQ ID NO:” (or the plural form “PEP NOs: and/or SEQ ID NOs:”) may be used to refer to a peptide or group of peptides that may include some with or without a SEQ ID NO:. For a peptide that has a SEQ ID NO: the phrase should be understood to refer to that peptide’s SEQ ID NO: and for a peptide that does not have a SEQ ID NO: (and only has a PEP NO:) that phrase should be understood to refer to that peptide’s PEP NO:. In the sequence listing a placeholder is inserted to ensure all peptides that have both a SEQ ID NO: and a PEP NO: have the same number assigned to both the SEQ ID NO: and the PEP NO:. For additional clarity PEP NOs: 199, 207, 636, 644, 756, 762, 766, 769, 771, 773, 782, 797, 811, 854, 860, 865, 869, 872, 874, 875 as well as 316 and 318-437 do not meet the criteria for sequence listing and where a SEQ ID NO: may appear to refer to one of these numbers the PEP NO: of the same number should be considered instead. All other PEP NOs: and/or SEQ ID NOs: may be referred to by either their PEP NO: and/or SEQ ID NO: and are included in the sequence listing.

Accordingly, in some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315. Each of these peptides was demonstrated to exhibit activity as a delta opioid receptor agonist in vitro.

Interestingly, it was discovered that retro-inverso variants of our delta opioid agonist peptides also exhibit delta opioid receptor agonist activity in vitro, since PEP NOs: and/or SEQ ID NOs: 305-315 are retro-inverso variants of the reference alignment provided by PEP NOs: and/or SEQ ID NOs: 1-304, and each of PEP NOs: and/or SEQ ID NOs: 305-315 exhibits delta opioid

receptor agonist activity. Accordingly, in some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 438-752 – which are retro-inverso forms of PEP NOs: and/or SEQ ID NOs: 1-315.

- In some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 16, 17, 24, 86, 87, 157, 162, 163, 164, 165, 166, 167, 170, 171, 173, 175, 177, 178, 179, 182, 183, 185, 186, or 187. This group of 24 peptides was studied in an animal model of analgesia, and all 24 peptides were found exhibit analgesic efficacy in vivo (none of the peptides tested in vivo failed to have an analgesic effect) - providing evidence that the in vitro delta opioid receptor agonist activity of the peptides of the present invention correlates with their in vivo analgesic activity. Furthermore, and importantly, the 24 peptides tested differed substantially from one another in their structure, size, length, and sequence - confirming that the ability to elicit in vivo analgesia is not unique to one peptide, or one narrow group of peptides, but rather appears to be a general property of the peptides invented.
- Analysis of the amino acid sequences of the peptides described above revealed certain common sequence motifs that could be described using consensus amino sequences. Accordingly, in some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 316-437, each of which consensus sequences has at least one variable amino acid position. Similarly, in some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 747-875, each of which consensus sequences represents a sequence motif that is shared by numerous of the peptides described herein.

The present invention also provides variants of the peptides described above. For example, in some embodiments, the present invention provides peptides comprising an amino acid sequence that is at least 90% identical to any one of PEP NOs: and/or SEQ ID NOs: 1-315, 438-752, or 747-875, provided that the variant peptides have delta opioid agonist activity. Numerous other types of variant peptide are also provided by the present invention, as described in other sections of this patent disclosure.

The present invention also provides compositions comprising the peptides described herein. For example, in some embodiments, the present invention provides pharmaceutical compositions comprising a peptide as described herein and at least one pharmaceutically acceptable carrier or excipient.

The present invention also provides various methods of using the peptides of the present invention. For example, in some embodiments, the present invention provides methods of activating a delta opioid receptor, such methods comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo, with a peptide as described herein.

- 5 Similarly, in some embodiments, the present invention provides methods of treating pain in subjects in need thereof, such methods comprising administering to such a subject an effective amount of a peptide as described herein.

For ease of reading the present specification, the following summary table of PEP NOs: and/or SEQ ID NOs: is provided:

10 **Table 1.** Summary table of PEP NOs and/or SEQ ID NOs:

PEP NO: and/or SEQ ID NO:	Summary description
1-315	Peptides (listed in Table 3): amino acid sequences of peptides synthesized and demonstrated to have delta opioid receptor agonist activity of at least 50% at or below 100 μ M.
316-437	Consensus sequences (listed in section 2.7 of the Detailed Description of the Invention): consensus amino acid sequences having variable "X" positions
438-752	Retro-inverso peptides (listed in Table 4): amino acid sequences of retro-inversos of PEP NOs: and/or SEQ ID NOs: 1-315
753-773	Consensus sequences (listed in section 2.4 of the Detailed Description of the Invention): consensus amino acid sequences having no variable positions (PEP NOs: and/or SEQ ID NOs: 747-752 are also sequences that are considered consensus sequences in in section 2.4)
774-875	Consensus sequences (listed in section 2.6 of the Detailed Description of the Invention): consensus amino acid sequences having no variable positions (PEP NOs: and/or SEQ ID NOs: 70, 126, 131, 135, 137, 138, 141 are also sequences are considered consensus sequences in in section 2.6)
876-882	N-terminal and C-terminal additions (listed in section 2.9 of the Detailed Description of the Invention)

These and other embodiments of the present invention are further described below.

BRIEF DESCRIPTION OF THE FIGURES

- 15 **Fig. 1A-F.** Amino acid sequences of 304 delta opioid receptor agonist peptides shown in Table 3 (PEP NOs: and/or SEQ ID NOs: 1-304) aligned according to sequence identity and numbered according to the aligned position. Positions are numbered from 1 through 20 (X₁ through X₂₀). Positions may contain one or more amino acids as well as other molecular elements.

- Fig. 1G.** Amino acid sequences of 11 delta opioid receptor agonist peptides shown in Table 3 (PEP NOs: and/or SEQ ID NOs: 305-315) aligned according to sequence identity and numbered according to the aligned position. Positions are numbered from 20 through 1 (X₂₀ through X₁) to demonstrate positional alignment with the reference alignment of PEP NOs: and/or SEQ ID NOs: 1-304, of which the reference alignment of PEP NOs: and/or SEQ ID NOs: 305-315 is a retro-inverso. Positions may contain one or more amino acids as well as other molecular elements.
- Fig. 2A.** An in vitro agonist response curve for a peptide having the amino acid sequence of PEP NO: and/or SEQ ID NO: 157 in a fluorescent cAMP assay, as detailed in Example 1.
- Fig. 2B.** An in vitro agonist response curve for a peptide having the amino acid sequence of PEP NO: and/or SEQ ID NO: 24 in a calcium flux assay, as detailed in Example 2.
- Fig. 2C.** An in vitro binding curve for a peptide having the amino acid sequence of PEP NO: and/or SEQ ID NO: 157 in a competitive radioligand assay, as detailed in Example 3.
- Fig. 3.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DSYGEVGVRQAPFPLSISCN (PEP NO: and/or SEQ ID NO: 1).
- Fig. 4.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DSYGEVGVRQAPFPSRASCN (PEP NO: and/or SEQ ID NO: 2).
- Fig. 5.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DSYGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 3).
- Fig. 6.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of RGDGEVGVRQAPFPLSISCN (PEP NO: and/or SEQ ID NO: 4).
- Fig. 7.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of RGDGEVGVRQAPFPLSISC (PEP NO: and/or SEQ ID NO: 5).
- Fig. 8.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of RGDGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 6).
- Fig. 9.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of RGDGEVGVRQAPYPSRASC (PEP NO: and/or SEQ ID NO: 7).
- Fig. 10.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of RGDGEVGVRQAPYLSRAFC (PEP NO: and/or SEQ ID NO: 8).
- Fig. 11.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DGDGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 9).
- Fig. 12.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of RGD SYGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 10).
- Fig. 13.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DSYGEVGVRQAPFPSRAS{c-amid-C} (PEP NO: and/or SEQ ID NO: 11).

- Fig. 14.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DSYGEVGVRQAPFPSRAS{c-amid-{dC}} (PEP NO: and/or SEQ ID NO: 12).
- Fig. 15.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {dβD}SYGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 13).
- Fig. 16.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of DSYGEVGVRQAPFPSRAS{dC} (PEP NO: and/or SEQ ID NO: 14).
- Fig. 17.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {dD}SYGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 15).
- Fig. 18.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-D}SYGEVGVRQAPFPSRAS{c-amid-C} (PEP NO: and/or SEQ ID NO: 16).
- Fig. 19.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}} (PEP NO: and/or SEQ ID NO: 17).
- Fig. 20.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {dD}SYGEVGVRQAPF{dP}SRASC (PEP NO: and/or SEQ ID NO: 18).
- Fig. 21.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {htt-cyclic-D}SYGEVGVRQAPFPSRASC (PEP NO: and/or SEQ ID NO: 19).
- Fig. 22.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-peg12-{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}} (PEP NO: and/or SEQ ID NO: 20).
- Fig. 23.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{dS}{c-amid-{dC}} (PEP NO: and/or SEQ ID NO: 24).
- Fig. 24.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-D}SYGEVGVRQAPFPS{r-pal-K}AS{c-amid-C} (PEP NO: and/or SEQ ID NO: 86).
- Fig. 25.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-ste-K}{dA}{dS}{c-amid-{dC}} (PEP NO: and/or SEQ ID NO: 87).
- Fig. 26.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{c-amid-{dS}} (PEP NO: and/or SEQ ID NO: 157).

- Fig. 27.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-D}SYGEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 162).
- Fig. 28.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-Y}GEVGVRQAPF{c-amid-P} (PEP NO: and/or SEQ ID NO: 163).
- Fig. 29.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-Y}GEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 164).
- Fig. 30.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-D}SYGEVGVRQAPF{c-amid-P} (PEP NO: and/or SEQ ID NO: 165).
- Fig. 31.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-Y}GEVGVRQAPFPS{c-amid-R} (PEP NO: and/or SEQ ID NO: 166).
- Fig. 32.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-Y}GEVGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 167).
- Fig. 33.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-E}VGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 170).
- Fig. 34.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-V}GVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 171).
- Fig. 35.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-Y}GEVGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 173).
- Fig. 36.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-Y}GEVGV{hR}QA{c-amid-P} (PEP NO: and/or SEQ ID NO: 175).
- Fig. 37.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-{dY}}GEVGV{hR}QA{c-amid-P} (PEP NO: and/or SEQ ID NO: 177).
- Fig. 38.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-{dY}}GEVGVRHA{c-amid-P} (PEP NO: and/or SEQ ID NO: 178).
- Fig. 39.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-Y}GEVGV{hR}HA{c-amid-P} (PEP NO: and/or SEQ ID NO: 179).
- Fig. 40.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-G}LMGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 182).
- Fig. 41.** An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-{dD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{c-amid-{dA}} (PEP NO: and/or SEQ ID NO: 183).

Fig. 42. An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-Y}GEVGVQRAPFPS{c-amid-{r-pal-K}} (PEP NO: and/or SEQ ID NO: 185).

Fig. 43. An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-pal-D}SYGEVGVQRAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 186).

Fig. 44. An example of a predicted or modeled chemical structure of a peptide having the amino acid sequence of {n-acet-D}SYGEVGVQRAPFPS{r-pal-K}A{c-amid-S} (PEP NO: and/or SEQ ID NO: 187).

DETAILED DESCRIPTION OF THE INVENTION

Some embodiments of the present invention are described in the “Summary of the Invention”, “Brief Description of the Figures”, “Examples”, “Claims,” and “Figures” sections of this patent disclosure. This “Detailed Description of the Invention” section provides certain additional embodiments, and certain additional description and details relating to embodiments described throughout the present patent disclosure and is intended to be read in conjunction with all other sections of the present patent disclosure.

For ease of reference, this Detailed Description of the Invention section is arranged using the following headings and subheadings:

Table 2. Headings and subheadings of the Detailed Description of the Invention

1	Definitions & Abbreviations
2	Peptides
2.1	PEP NOs: and/or SEQ ID NOs: 1-315
2.2	Activity Groups
2.3	Modification Groups
2.4	Sequence Groups
2.5	Sequence Groups with Variants
2.7	Consensus Sequences
2.8	Retro-inverso Sequences
2.9	Variant Peptides
2.9.1	Deletion Variants
2.9.2	Fragment Variants
2.9.3	Addition Variants
2.9.4	Substitution Variants
2.9.5	Percent Identity Variants
2.9.6	Activity Variants and Groups
2.9.7	Modification Variants
3	DOR Binding & Agonist Activity
4	Methods of Manufacture
4.1	Manufacture by Recombinant Peptide Expression

4.2	Manufacture by Synthesis
5	Nucleic Acid Molecules, Vectors, and Host Cells
6	Compositions
7	Kits
8	Methods of Use and Methods of Treatment
9	Additional Embodiments

The headings and subheadings used herein are not intended to limit the scope of the invention in any way. All sections of this patent disclosure should be read in conjunction with all other sections of the patent disclosure. Similarly, one of ordinary skill in the art will understand that the various embodiments of the present invention can be combined in various different ways. All such combinations of embodiments fall within the scope of the present invention.

1. Definitions & Abbreviations

In order that the present invention can be more readily understood, certain terms are defined below. Additional definitions are set forth throughout the disclosure where the terms are used.

Unless defined otherwise, or a specific meaning is clear from the context of use, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention is related. The Dictionary of Cell and Molecular Biology (5th ed. J.M. Lackie ed., 2013), the Oxford Dictionary of Biochemistry and Molecular Biology (2d ed. R. Cammack et al. eds., 2008), and The Concise Dictionary of Biomedicine and Molecular Biology (2d ed. P-S. Juo, 2002) can provide one of skill with general definitions of some of the terms used herein.

Units, prefixes, and symbols as used herein are denoted in their Système International de Unites (SI) accepted form. Numeric ranges provided herein are inclusive of the numbers defining the range.

As used herein, the singular forms “a,” “an,” and “the” include plural referents, unless the context clearly dictates otherwise. The terms “a” (or “an”) as well as the terms “one or more” and “at least one” can be used interchangeably.

As used herein, “and/or” is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term “and/or” as used in a phrase such as “A and/or B” is intended to include A and B, A or B, A (alone), and B (alone). Likewise, the term “and/or” as used in a phrase such as “A, B, and/or C” is intended to include A, B, and C; A, B, or C; A or B; A or C; B or C; A and B; A and C; B and C; A (alone); B (alone); and C (alone).

As used herein the terms “about” and “approximately,” when used in relation to numerical values, mean within + or – 10% of the stated value.

As used herein, the terms “affinity” and “binding affinity” refer to the strength of the sum-total of non-covalent interactions between a binding site on a first molecule (e.g., a peptide as described herein) and a second molecule (e.g., a delta opioid receptor). Unless indicated otherwise, as used herein, “binding affinity” refers to intrinsic binding affinity which reflects a 1:1 interaction between members of a binding pair (e.g., a peptide and a delta opioid receptor). The affinity of a molecule for another molecule can be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art (such as radiolabeled assays) or as described herein.

As used herein, the term “agonist” refers to a molecule (e.g., a peptide) with the ability to produce a detectable, measurable, or observable activation of a specified receptor (e.g., a delta opioid receptor), for example in an in vitro or in vivo assay.

As used herein, the term “amino acid” includes all canonical and non-canonical amino acids known in the art, and includes both naturally occurring and non-naturally occurring amino acids known in the art. As used herein, the term “naturally occurring” as it refers to an amino acid refers to the twenty canonical amino acids encoded by the human genetic code (i.e., Alanine (Ala, A), arginine (Arg, R), asparagine (Asn, N), aspartic acid (Asp, D), cysteine (Cys, C), glutamine (Gln, Q), glutamic acid (Glu, E), glycine (Gly, G), histidine (His, H), isoleucine (Ile, I), leucine (Leu, L), lysine (Lys, K), methionine (Met, M), phenylalanine (Phe, F), proline (Pro, P), serine (Ser, S), threonine (Thr, T), tryptophan (Trp, W), tyrosine (Tyr, Y), and valine (Val, V)). Examples of non-naturally occurring and/or non-canonical amino acids include but are not limited to citrulline (Cit), hydroxyproline (Hyp), norleucine (Nle), 3-nitrotyrosine, nitroarginine, ornithine (Orn), naphthylalanine (Nal), Abu, DAB, methionine sulfoxide or methionine sulfone.

In some embodiments, the peptides of the present invention may contain one or more “modified amino acids.” As used herein the term “modified” when used in relation to amino acids refers to an amino acid that differs chemically from the form of that amino acid that is encoded by the genetic code or that typically exists in nature. Examples of modified amino acids include but are not limited to amino acids having D chirality as opposed to L chirality, amino acids in their beta form as opposed to alpha form, homo amino acids (e.g., homoalanine), gamma amino acids, beta homo amino acids, N-methyl amino acids, alpha-methyl amino acids, beta-methyl amino acids, fluoro-amino acids, amino acids that are acetylated, amino acids that are acylated, amino acids that are fatty acylated, amino acids that are amidated, amino acids that are methylated, amino acids that are phosphorylated, amino acids that are palmitoylated, amino acids that are glycosylated, amino acids that have undergone stearic acid conjugation, amino acids that are pegylated, amino acids conjugated to deoxyribonucleic acids or ribonucleic acids or

oligonucleotides or polynucleotides, amino acids that have been labelled or tagged (e.g. using a fluorescent or isotopic label or tag), amino acids that have an added protecting group, and amino acids altered using other manipulations or modifications known in the art.

Further information regarding “modified amino acids” that may be used in the peptides of the present invention is provided elsewhere in this patent disclosure (see, e.g., the description under the subheading “Peptides” regarding “modified” amino acids). Other modified, non-naturally occurring, and non-canonical amino acids are known in the art, for example as described in Sandberg et al., “*New Chemical Descriptors Relevant for the Design of Biologically Active Peptides. A Multivariate Characterization of 87 Amino Acids;*” J. Med. Chem.; 1998; 41(14); pp. 2481-91).

Amino acids are typically referred to using either their accepted three-letter or one-letter symbols as recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Amino acids are referred to herein using their one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Modified amino acids are referred to herein using their one-letter symbol in conjunction with one or more prefixes, as described further in the “Detailed Description of the Invention” section of this patent disclosure.

The terms “comprising,” “consisting of,” and/or “consisting essentially of” are used herein consistently with their accepted meanings according to U.S. patent law. Wherever embodiments are described with the language “comprising,” otherwise analogous embodiments described in terms of “consisting of,” and/or “consisting essentially of” are also intended and included within the scope of the invention.

The terms “consensus” or “consensus sequence” or “consensus amino acid sequence,” as used herein, refer to an amino acid sequence obtained by comparing multiple aligned amino acid sequences to identify shared sequence motifs. For example, the present invention provides various consensus amino acid sequences obtained by aligning and comparing the amino acid sequences of peptides having the sequences of PEP NOs: and/or SEQ ID NOs: 1-315, or by comparing subgroups of peptides from among PEP NOs: and/or SEQ ID NOs: 1-315, and identifying shared sequence motifs. In some cases, consensus sequences are identified in which the amino acid occurring at each aligned position is the same, in which case the amino acid at each position of the consensus sequence is specified (such as, for example, the consensus amino acid sequences PEP NOs: and/or SEQ ID NOs: 747-875 as provided herein). In some cases, consensus sequences are identified in which one or more positions can vary in terms of the amino acid occurring at that position, in which case one or more of the positions in the consensus sequence is identified as a variable “X” amino acid residue, with the possible amino acids that

can occur at the variable “X” position being specified (such as, for example, PEP NOs: and/or SEQ ID NOs: 316-437 as provided herein). Amino acid consensus sequences are useful because they provide a method of correlating the structure of a group of proteins or peptides to their biological function. For example, the consensus amino acid sequences provided herein represent
5 common structural motifs that are believed to be correlated to the DOR agonist activity of the peptides that contain them.

As used herein, the abbreviation “DOR” refers to a delta opioid receptor. In some embodiments of the present invention, the DOR is a mammalian DOR. In some embodiments of the present invention, the DOR is a rodent DOR. In some embodiments, of the present invention, the DOR is
10 a non-human primate DOR. In some embodiments of the present invention, the DOR is a human DOR.

As used herein, the term “delta opioid agonist” or “DOR agonist” refers to a molecule that has agonist activity at the delta opioid receptor that is detectable in any suitable assay for delta opioid agonism known in the art, such as, for example, detection of a variety of downstream
15 effects including but not limited to: effects on cyclic adenosine monophosphate (“cAMP”) (e.g., cAMP production), which can be detected using methods known in the art such as the assay in Example 1, effects on beta-arrestin (e.g., beta-arrestin recruitment), which can be detected using methods known in the art such as the assay in Example 4, effects on calcium (e.g., calcium flux), which can be detected using methods known in the art such as the assay in Example 2, or effects
20 on receptor conformational changes and/or receptor internalization, which can be detected using methods known in the art such as the assay in Example 4.

As used herein, the term “biased DOR agonist” refers to a molecule (such as a peptide) that preferentially activates (as measured by lower EC₅₀ and/or greater maximal effect) one or more effects downstream of DOR agonism (as are known in the art (e.g. cAMP production, beta
25 arrestin recruitment, receptor internalization, calcium flux, and/or others)) relative to one or more other effects downstream of DOR agonism.

As used herein when referring to a peptide, the terms “stable” or “exhibiting stability” and the like refer to the peptide exhibiting less than 10% degradation or a less than 10% decrease in biological activity under the stated conditions (e.g., in a stated composition, and/or for a stated
30 time, and/or at a stated temperature) unless another specific stability level is stated. In some embodiments the level of stability is assessed using one or more of the stability assays described in Examples section of this patent disclosure, which include stability assays based on assessing peptide degradation by HPLC, and stability assays based on assessing biological activity in vivo or in vitro.

As used herein, the term “effective amount,” when used in relation to the DOR agonist peptides of the present invention, refers to an amount of a DOR agonist peptide that is sufficient to have activity as an agonist of a DOR Example 1, or to achieve detectable, measurable, or observable agonism of a DOR, or to achieve a detectable, measurable, or observable biological effect or treatment effect (see definition of “treatment” below defined below), in the stated situation. The amount of a given peptide, or composition comprising such a peptide, that is an “effective amount” may depend on variety of factors including, but not limited to, the species of the subject (e.g., whether a human or some other animal species), the age of the subject, the sex of the subject, the weight of the subject, the formulation of the peptide, the route of administration of the peptide, the planned dosing regimen, etc. The effective amount (which may be a range of effective amounts) can be determined by standard techniques, for example using in vitro assays and/or in vivo assays in the intended subject species or any suitable animal model species. Suitable methods for determining an effective amount include, but are not limited to, dose-escalation studies, extrapolation from dose-response curves, and/or extrapolation from other data derived from in vitro and/or in vivo model systems. In some embodiments, the effective amount may be determined according to the judgment of a medical or veterinary practitioner based on the specific circumstances.

The term “selective agonists of the delta opioid receptor” or “selective delta opioid receptor agonists” as used herein denotes any compound which has a higher binding affinity for (or a higher agonist activity at) the delta-opioid receptor than for/at any other opioid receptor (such as at the mu opioid receptor). Preferably the compounds have a binding affinity or an agonist activity that is at least 2, or more preferably at least 5, or more preferably at least 10, or more preferably at least 20, or more preferably at least 50, or more preferably at least 100 or more preferably at least 200, or more preferably at least 500, or more preferably at least 1000 times higher for the delta-opioid receptor than for any other opioid receptor (such as the mu opioid receptor). Such binding affinity levels and agonist activity levels can be determined by methods known in the art including by the assay described in Example 3 (in the case of binding activity) or Example 1, or Example 2, or Example 4 (in the case of agonist activity). Similarly, in vivo selectivity for the delta opioid receptor can be determined using any suitable methods known in the art, for example using genetic knockout animals that lack expression of an opioid receptor (e.g., DOR knockouts and/or knockouts of other opioid receptors (such as at the mu opioid receptor)), or using antagonists or competitive agonists having known specificity for a given opioid receptor (such as the DOR or mu opioid receptor).

As used herein, the terms “exemplary” or “e.g.” or “for example” or “such as” mean serving as an example, instance, or illustration. These terms are non-limiting and are not intended to denote preferred embodiments.

As used herein, the terms “gastrointestinal site of action” or “GI site of action” mean, when
5 referring to an orally administered DOR agonist peptide as described herein, having activity primarily at DORs within or in the vicinity of to the gastrointestinal (GI) tract rather than at DORs systemically or elsewhere in the body (such as in the brain). A GI site of action can be demonstrated using any suitable method known in the art, or any method as described herein. For example, a GI site of action of a peptide of the present invention is demonstrated when the
10 therapeutic efficacy of the peptide is proportional to the dose of that peptide that is administered orally, but not proportional to and independent of the level of that peptide in blood circulation following oral administration (i.e., independent of systemic exposure).

As used herein, the terms “identical” and “percent identity” when used to refer to a comparison between two peptides, refer, respectively, to two peptides that have the same amino acid
15 sequence and the same amino acid modifications (i.e. they are “identical”) or that have a specified percentage of amino acid residues that have the same amino acid sequence and the same amino acid modifications (i.e. they have the stated “percent identity”) when the two peptides are compared and aligned (introducing gaps or insertions, if necessary) for maximum correspondence. For example, if two 10 amino acid peptides have the same amino acid sequence
20 but in one peptide, and not the other, one amino acid is acetylated or one amino acids has D chirality instead of L chirality, the two peptides are considered to be 90% identical or to have 90% identity. Percent identity can be determined or measured using sequence comparison software or algorithms or by visual inspection. Various algorithms and software are known in the art that can be used to obtain alignments of amino acid sequences and to calculate percent
25 identity.

As used herein, the term “isolated” refers to molecules (e.g., peptides) that are not within a living subject or cell and are typically in a form not found in nature. In some embodiments, an isolated molecule may have been purified to a degree that it is not in a form in which it is found in nature. In some embodiments, a molecule that is isolated is “substantially pure.” In some embodiments,
30 the peptides described herein are isolated peptides.

As used herein, the term “peptide” refers to a polymer of amino acids linked via peptide bond(s) regardless of conformation or internal linkages. Thus, the term “peptide” includes linear, branched, disulfide bridged, and cyclized peptides, as well as peptides having any other topology known in the art. The peptides of the present invention can be modified and/or can include

modified amino acids and/or can be interrupted by and/or conjugated with non-amino acids.

Peptides may be represented herein using strings of amino acid abbreviations (i.e., amino acid sequences). Such amino acid sequences may be referred to using a sequence identification number (SEQ ID NO:) as per the sequence listing associated with this application) or a

- 5 corresponding peptide number (PEP NO:), wherein the terms SEQ ID NO: 1 and PEP NO:1 refer to the same peptide having the same amino acid sequence, and the terms SEQ ID NO: 2 and PEP NO:2 refer to the same peptide having the same amino acid sequence, and so on for all SEQ ID NOs: and PEP NOs:. The two terms may thus be used interchangeably.

- Unless stated otherwise, peptides represented by their amino acid sequence are presented with
10 the N-terminus on the left and the sequence is written from the N-terminus to the C-terminus. Peptides may also be represented herein by their chemical structure. A peptide may be comprised of any number of amino acids but preferably less than 200 amino acids such as fewer than 200 amino acids, fewer than 100 amino acids, fewer than 50 amino acids, fewer than 40 amino acids, fewer than 30 amino acids, fewer than 20 amino acids, fewer than 15 amino acids, fewer than 10
15 amino acids, 3-20 amino acids, 4-20 amino acids, 5-20 amino acids, 6-20 amino acids, 7-20 amino acids, 8-20 amino acids, 9-20 amino acids, or 10-20 amino acids.

- As used herein, the term “pharmaceutical composition” refers to a composition that is in such form as to permit the biological activity of the active agent(s) contained therein (e.g., peptide(s)), and that contain no additional components that are unacceptably toxic to a subject to which the
20 composition may be administered. In some embodiments, such compositions may be sterile.

- As used herein, the term “potency” is used consistent with its accepted meaning in the art and is a measure of the activity of a given agent (e.g., a peptide as described herein) expressed in terms of the amount required to produce a stated effect (e.g., detectable activation of the DOR). A highly potent agent produces the stated effect at a low concentration, while an agent having
25 lower potency produces the stated effect only at higher concentrations. The “potency” of the peptides described herein may be expressed using any suitable measure known in the art. For example, the potency of the peptides may be referred to in terms of their “EC₅₀” values or “IC₅₀” values. For example, in a functional assay, the EC₅₀ may be the concentration of the peptide that induces a biological response that is 50% of the peptide’s maximum biological response in the
30 stated functional assay. For example, in the case of the present invention, the EC₅₀ of a peptide described herein is the concentration of the peptide that induces 50% of that peptide’s maximal DOR agonism. As an alternative to expressing potency using EC₅₀ values, the potency of the peptides of the present invention may also be described herein in terms of the % of DOR agonism relative to a known standard (e.g., D-Pen2,5 -Enkephalin (“DPDPE”)) observed at a

given concentration of the peptide or at or below a given concentration of the peptide. For example, a peptide of the present invention may be described as having DOR agonist activity of at least 50% at a concentration at or below 10 μ M, or may be described as having DOR agonist activity of at least 90% at a concentration at or below 10 μ M.

5 As used herein, the term “primate” refers to any mammal of the group that includes the lemurs, lorises, tarsiers, monkeys, apes, and humans.

As used herein, the term “retro-inverso” refers to a peptide that has amino acids in the reverse order and where each amino acid has changed chirality (i.e., from L to D or from D to L) relative to a stated reference amino acid sequence, disregarding N-terminal and C-terminal modifications
10 of the reference amino acid sequence. The stated reference amino acid sequence may specify all amino acid residues or it may be a consensus amino acid sequence in which some of the amino acid residues can vary in a specified manner.

As used herein, the term “subject” refers to an individual for whom prophylaxis or treatment using a peptide, composition, or method as described herein is desired, needed or performed. As
15 used herein, a subject “in need thereof” is a subject who could reasonably be expected to benefit from prophylaxis or treatment using a peptide, composition, or method as described – for example as determined by a medical professional. In some embodiments, the subject is any mammalian subject, including, but not limited to, humans (male and/or female), non-human primates, dogs, cats, rodents (such as rats, mice and guinea pigs), cows, pigs, sheep, goats,
20 horses, and the like – including all mammalian animal species used in animal husbandry, as well as animals kept as pets and in zoos, and animals used in preclinical testing. In some embodiments, the subject may be a juvenile. In some embodiments, the subject may be an adult. In some embodiments, the subject may be an elderly adult.

As used herein, the term “substantially pure” when used in reference to a peptide refers to at
25 least about 70%, preferably at least about 80%, more preferably at least about 90%, and most preferably at least about 95%, 98%, 99%, or 99.9% purity of the peptide.

As used herein, the terms “treat,” “treating,” and “treatment” refer to achieving, and/or performing a method that achieves, a detectable, measurable, or observable improvement in one or more clinical parameters or symptoms. For example, in the case of pain, “treatment” refers to
30 achieving, and/or performing a method that achieves, a detectable, measurable, or observable analgesic effect (e.g., comprising an improvement in pain, a reduction in pain, an elimination of pain, a prevention of pain, a lessened duration of pain, etc.). Thus, the phrases “method of treating pain” and “method of inducing analgesia” (and grammatical variations of these phrases) may be used interchangeably herein.

The term “means” is used herein consistently with its usage in U.S. patent law, and shall be given its broadest possible interpretation in accordance with 35 U.S.C. section 112(f).

Accordingly, a claim incorporating the term “means” shall cover all structures, materials, or acts described herein, and all equivalents thereof. Further, the structures, materials, or acts shall
5 include all of those described in the Summary of the Invention, Brief Description of the Figures, Figures, Detailed Description of the Invention, Examples, Claims, Abstract, and Sequence Listing. It is intended that the peptides of the present invention may also be referred to as a means for achieving a function or effect as described herein. Thus, whenever an embodiment of the present invention is described without using “means” language, it is to be understood that an
10 analogous embodiment, described as a “means” for achieving a certain function or effect, is also contemplated and falls within the scope of the present invention.

Other terms are defined elsewhere in this patent disclosure, or else are used in accordance with their accepted meaning in the art.

2. Peptides

15 The present invention provides a number of novel peptides.

In some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1-315 (as described in more detail in section 2.1 below and elsewhere herein). In some embodiments, the present invention provides peptides that can be described using the consensus amino acid sequence of any of PEP NO: and/or
20 SEQ ID NO: 316-437 (as described in more detail in section 2.7 below and elsewhere herein). In some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 438-752 (as described in more detail in section 2.8 below and elsewhere herein). In some embodiments, the present invention provides peptides that comprise the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 747-875 (as
25 described in more detail in section 2.4 below and elsewhere herein). Whenever a peptide is referred to herein in terms of its PEP NO: and/or SEQ ID NO:, without further qualification, the peptide has the amino acid residues, amino acid modifications, and other peptide attributes (such as cyclization) specified in the description of that PEP NO: and/or SEQ ID NO: that is provided herein (such as in Table 3, below). In some embodiments, the present invention provides peptides
30 having the chemical structures provided in Figs. 3-44.

In some embodiments, the present invention provides “variant” peptides that differ from, or that comprise a peptide that differs from, any of the amino acid sequences provided herein. The differences between the variant peptides and peptides that comprise each PEP NO: and/or SEQ ID

NO: can occur at various levels, including at the level of the amino acid residues (e.g., variant peptides may comprise amino acid substitutions, deletions, or additions as compared to that of any specified PEP NO: and/or SEQ ID NO:), at the level of amino acid modifications (e.g., variant peptides may have modifications added or removed as compared to any specified PEP NO: and/or SEQ ID NO:), or may include different modifications from those in any specified any specified PEP NO: and/or SEQ ID NO:), and at the level of other peptide attributes (such as cyclization, dimerization, multimerization, and the like). Examples of such variant peptides are described in more detail in section 2.9 below and elsewhere herein.

In some embodiments, the peptides of the present invention have a maximum length of 3 amino acids, or 4 amino acids, or 5 amino acids, or 6 amino acids, or 7 amino acids, or 8 amino acids, or 9 amino acids, or 10 amino acids, or 11 amino acids, or 12 amino acids, or 13 amino acids, or 14 amino acids, or 15 amino acids, or 16 amino acids, or 17 amino acids, or 18 amino acids, or 19 amino acids, or 20 amino acids, or 21 amino acids, or 22 amino acids, or 23 amino acids, or 24 amino acids, or 25 amino acids, or 26 amino acids, or 27 amino acids, or 28 amino acids, or 29 amino acids, or 30 amino acids.

In some embodiments, the peptides of the present invention provide novel tools for studying the delta opioid receptor's role in human pathophysiology.

In some embodiments, the peptides of the present invention have delta opioid agonist activity. In some embodiments, the peptides of the present invention have delta opioid agonist activity in animal models. In some embodiments, the peptides of the present invention have delta opioid agonist activity in primates. In some embodiments, the peptides of the present invention have delta opioid agonist activity in non-human primates. In some embodiments, the peptides of the present invention have delta opioid agonist activity in human subjects.

In some embodiments, the peptides of the present invention act predominantly through agonism of the delta opioid receptor and not through agonism of the mu opioid receptor. In some embodiments, the peptides of the present invention act predominantly through agonism of the delta opioid receptor and not through agonism of the mu opioid receptor in animal models. In some embodiments, the peptides of the present invention act predominantly through agonism of the delta opioid receptor and not through agonism of the mu opioid receptor in primates. In some embodiments, the peptides of the present invention act predominantly through agonism of the delta opioid receptor and not through agonism of the mu opioid receptor in non-human primates. In some embodiments, the peptides of the present invention act predominantly through agonism of the delta opioid receptor and not through agonism of the mu opioid receptor in human subjects.

In some embodiments, the peptides of the present invention are selective delta opioid receptor agonists. In some embodiments, the peptides of the present invention are selective delta opioid receptor agonists in animal models. In some embodiments, the peptides of the present invention are selective delta opioid receptor agonists in primates. In some embodiments, the peptides of the present invention are selective delta opioid receptor agonists in non-human primates. In some embodiments, the peptides of the present invention are selective delta opioid receptor agonists in human subjects.

In some embodiments, the peptides of the present invention are specific delta opioid receptor agonists. In some embodiments, the peptides of the present invention are specific delta opioid receptor agonists in animal models. In some embodiments, the peptides of the present invention are specific delta opioid receptor agonists in primates. In some embodiments, the peptides of the present invention are specific delta opioid receptor agonists in non-human primates. In some embodiments, the peptides of the present invention are specific delta opioid receptor agonists in human subjects.

In some embodiments, the peptides of the present invention exhibit analgesic efficacy in animal models. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in a rodent model of pain such as that described in Example 5. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in primates. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in non-human primates. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in human subjects.

In some embodiments, the peptides of the present invention exhibit analgesic efficacy in animal models mediated by DOR agonism. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in rodent models mediated by DOR agonism. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in primates mediated by DOR agonism. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in non-human primates mediated by DOR agonism. In some embodiments, the peptides of the present invention exhibit analgesic efficacy in human subjects mediated by DOR agonism. In some embodiments, mediation by DOR agonism is determined through use of genetic knockout animals (e.g., DOR knockouts) and/or other methods known in the art. In some embodiments, mediation by DOR agonism is determined through use of known DOR specific antagonists and methods known in the art.

In some embodiments, the peptides of the present invention exhibit analgesic efficacy in a range of animal models such as animal models of acute mechanical pain, acute thermal pain, inflammatory pain, visceral pain, and/or neuropathic pain.

In some embodiments, the peptides of the present invention exhibit oral efficacy in animal models. In some embodiments, the peptides of the present invention exhibit oral efficacy in primates. In some embodiments, the peptides of the present invention exhibit oral efficacy in non-human primates. In some embodiments, the peptides of the present invention exhibit oral efficacy in
5 human subjects.

In some embodiments, the peptides of the present invention exhibit oral bioavailability in animal models. In some embodiments, the peptides of the present invention exhibit oral bioavailability in primates. In some embodiments, the peptides of the present invention exhibit oral bioavailability in non-human primates. In some embodiments, the peptides of the present invention exhibit oral
10 bioavailability in human subjects.

In some embodiments, the peptides of the present invention have a site of action that is not in the central nervous system. This is demonstrated by any methods known in the art including by use of conditional knockouts such as those utilizing Cre recombinase as is known in the art.

In some embodiments, the peptides of the present invention have a GI site of action. This is
15 demonstrated by any methods known in the art including by demonstration of effect (such as analgesic efficacy) proportional to oral dose but not proportional to systemic exposure.

In some embodiments, the peptides of the present invention provide analgesic efficacy lasting a clinically useful time. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting a clinically useful time when administered orally. In some embodiments,
20 the peptides of the present invention provide analgesic efficacy lasting about 2-6 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 2-12 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 2-18 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 2-24 hours. In some embodiments, the peptides of the present
25 invention provide analgesic efficacy lasting about 6-12 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 6-18 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 6-24 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 12-18 hours. In some embodiments, the peptides of the present
30 invention provide analgesic efficacy lasting about 12-24 hours. In some embodiments, the peptides of the present invention provide analgesic efficacy lasting about 18-24 hours.

In some embodiments, the peptides of the present invention are safe for administration to living subjects. In some embodiments, the peptides of the present invention are safe for administration

to primates. In some embodiments, the peptides of the present invention are safe for administration to non-human primates. In some embodiments, the peptides of the present invention are safe for administration to human subjects.

5 In some embodiments, the peptides of the present invention do not cause convulsions in living subjects. In some embodiments, the peptides of the present invention do not cause convulsions in primates. In some embodiments, the peptides of the present invention do not cause convulsions in non-human primates. In some embodiments, the peptides of the present invention do not cause convulsions in human subjects.

10 In some embodiments, the peptides of the present invention do not cause undesirable neurological effects such as narcotic effects in living subjects. In some embodiments, the peptides of the present invention do not cause undesirable neurological effects such as narcotic effects in primates. In some embodiments, the peptides of the present invention do not cause undesirable neurological effects such as narcotic effects in non-human primates. In some embodiments, the peptides of the present invention do not cause undesirable neurological effects such as narcotic effects in human subjects.

15 In some embodiments, the peptides of the present invention do not induce tolerance following repeated administration and/or maintain clinical efficacy following repeated administration in living subjects. In some embodiments, the peptides of the present invention do not induce tolerance following repeated administration and/or maintain clinical efficacy following repeated administration in primates. In some embodiments, the peptides of the present invention do not induce tolerance following repeated administration and/or maintain clinical efficacy following repeated administration in non-human primates. In some embodiments, the peptides of the present invention do not induce tolerance following repeated administration and/or maintain clinical efficacy following repeated administration in human subjects.

25 In some embodiments, the peptides of the present invention are not addictive in living subjects. In some embodiments, the peptides of the present invention are not addictive in primates. In some embodiments, the peptides of the present invention are not addictive in non-human primates. In some embodiments, the peptides of the present invention are not addictive in human subjects.

30 In some embodiments, the peptides of the present invention are stable as a solid (e.g. a lyophilized powder) for up to 1 hour at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable as a solid (e.g. a lyophilized powder) for up to 24 hours at less than -15°C, or at 0 to 4°C, or at 4 to

25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable as a solid (e.g. a lyophilized powder) for up to 1 week at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable as a solid (e.g. a lyophilized powder) for up to 1 month at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable as a solid (e.g. a lyophilized powder) for up to 6 months at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable as a solid (e.g. a lyophilized powder) as described in Example 7.

In some embodiments, the peptides of the present invention are stable in an aqueous solution (e.g. in solution with water) for up to 1 hour at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in an aqueous solution (e.g. in solution with water) for up to 24 hours at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in an aqueous solution (e.g. in solution with water) for up to 1 week at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in an aqueous solution (e.g. in solution with water) for up to 1 month at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in an aqueous solution (e.g. in solution with water) for up to 6 months at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C.

In some embodiments, the peptides of the present invention are stable in a non-aqueous solution for up to 1 hour at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C,

or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in a non-aqueous solution for up to 24 hours at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in a non-aqueous solution for up to 1 week at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in a non-aqueous solution for up to 1 month at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C. In some embodiments, the peptides of the present invention are stable in a non-aqueous solution for up to 6 months at less than -15°C, or at 0 to 4°C, or at 4 to 25°C, or at 25 to 40°C, or at 40 to 70°C, or at 70 to 90°C, or at 90 to 100°C, or at 100 to 110°C, or at -20 to 25°C, or at -20 to 4°C, or at -20 to 40°C.

In some embodiments, the peptides of the present invention are stable under acidic conditions such as described in Example 7. In some embodiments, the peptides of the present invention are stable in a peroxide solution as described in Example 7. In some embodiments, the peptides of the present invention are stable under ultraviolet light as described in Example 7.

In the embodiments described above, the peptides exhibit less than 10% degradation or a less than 10% decrease in biological activity under the stated conditions - as described in the Definitions & Abbreviations section of this patent disclosure relating to stability. However, in some embodiments, the peptides of the present invention exhibit even higher levels of stability under the conditions stated above. For example, in some embodiments the peptides of the invention exhibit less than 5% degradation or a less than 5% decrease in biological activity under the conditions stated above. In some embodiments the peptides of the invention exhibit less than 4% degradation or a less than 4% decrease in biological activity under the conditions stated above. In some embodiments the peptides of the invention exhibit less than 3% degradation or a less than 3% decrease in biological activity under the conditions stated above. In some embodiments the peptides of the invention exhibit less than 2% degradation or a less than 2% decrease in biological activity under the conditions stated above. In some embodiments the peptides of the invention exhibit less than 1% degradation or a less than 1% decrease in biological activity under the conditions stated above.

Additionally, in some embodiments, the peptides of the present invention exhibit lower levels of stability under the conditions stated above. In the embodiments described above, the peptides exhibit less than 90% degradation or a less than 90% decrease in biological activity under the

stated conditions. In the embodiments described above, the peptides exhibit less than 80% degradation or a less than 80% decrease in biological activity under the stated conditions. In the embodiments described above, the peptides exhibit less than 70% degradation or a less than 70% decrease in biological activity under the stated conditions. In the embodiments described above, the peptides exhibit less than 60% degradation or a less than 60% decrease in biological activity under the stated conditions. In the embodiments described above, the peptides exhibit less than 50% degradation or a less than 50% decrease in biological activity under the stated conditions. In the embodiments described above, the peptides exhibit less than 40% degradation or a less than 40% decrease in biological activity under the stated conditions. In the embodiments described above, the peptides exhibit less than 30% degradation or a less than 30% decrease in biological activity under the stated conditions. In the embodiments described above, the peptides exhibit less than 20% degradation or a less than 20% decrease in biological activity under the stated conditions.

In some embodiments, the peptides of the present invention are biased DOR agonists. In some embodiments, the peptides of the present invention exhibit preferential activation of one effect downstream of DOR activation as compared to another effect downstream of DOR activation. In some embodiments the peptides of the present invention are biased DOR agonists and have higher potency and/or activity at the DOR in a cAMP assay than in a beta arrestin assay. In some embodiments, the EC₅₀ of the peptide at the DOR in a beta arrestin assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-1000x, or 1000-10000x that in a cAMP assay. In some embodiments, the maximal effect of the peptide at the DOR in a cAMP assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x, or 300-1000x, or 1000-10000x that in a beta arrestin assay.

In some embodiments, the peptides of the present invention are biased DOR agonists and have higher potency and/or activity at the DOR in a calcium flux assay than in a beta arrestin assay. In some embodiments, the EC₅₀ of the peptide at the DOR in a beta arrestin assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x, or 300-1000x, or 1000-10000x that in a calcium flux assay. In some embodiments, the maximal effect of the peptide at the DOR in a calcium flux assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x, or 300-1000x, or 1000-10000x that in a beta arrestin assay.

In some embodiments, the peptides of the present invention are biased DOR agonists and have higher potency and/or activity at the DOR in a cAMP assay than in a receptor internalization assay. In some embodiments, the EC₅₀ of the peptide at the DOR in a receptor internalization assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x,

or 300-1000x, or 1000-10000x that in a cAMP assay. In some embodiments, the maximal effect of the peptide at the DOR in a receptor cAMP assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x, or 300-1000x, or 1000-10000x that in an internalization assay.

- 5 In some embodiments, the peptides of the present invention are biased DOR agonists and have higher potency and/or activity at the DOR in a calcium flux assay than in a receptor internalization assay. In some embodiments, the EC₅₀ of the peptide at the DOR in a receptor internalization assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x, or 300-1000x, or 1000-10000x that in a calcium flux assay. In some embodiments, the
- 10 maximal effect of the peptide at the DOR in a calcium flux assay is 1-1.2x, or 1.2-1.5x, or 1.5-1.75x, or 1.75-2x, or 2-5x, or 5-10x, or 10-50x, or 50-100x, or 100-300x, or 300-1000x, or 1000-10000x that in a receptor internalization assay.

Further details of the peptides of the present invention are provided below.

2.1. PEP NOs: and/or SEQ ID NOs: 1-315

- 15 Table 3 provides the amino acid sequences of 315 peptides (PEP NOs: and/or SEQ ID NOs: 1-315). Each of these peptides was synthesized and demonstrated to have delta opioid receptor agonist activity of at least 50% at or below 100 μ M, as described in Example 1.

Table 3. Amino acid sequences of PEP NOs: and/or SEQ ID NOs: 1-315

SEQ ID NO:	PEP NO:	Amino acid sequence	% Activity at 100 μ M
1	1	DSYGEVGVVRQAPFPLSISCN	99%
2	2	DSYGEVGVVRQAPFPSRASCN	99%
3	3	DSYGEVGVVRQAPFPSRASC	99%
4	4	RGDGEVGVVRQAPFPLSISCN	98%
5	5	RGDGEVGVVRQAPFPLSISC	99%
6	6	RGDGEVGVVRQAPFPSRASC	101%
7	7	RGDGEVGVVRQAPYPSRASC	100%
8	8	RGDGEVGVVRQAPYLSRAFC	98%
9	9	DGDGEVGVVRQAPFPSRASC	98%
10	10	RGDSYGEVGVVRQAPFPSRASC	103%
11	11	DSYGEVGVVRQAPFPSRAS{c-amid-C}	100%
12	12	DSYGEVGVVRQAPFPSRAS{c-amid-{dC}}	101%
13	13	{d β D}SYGEVGVVRQAPFPSRASC	101%
14	14	DSYGEVGVVRQAPFPSRAS{dC}	100%
15	15	{dD}SYGEVGVVRQAPFPSRASC	100%
16	16	{n-acet-D}SYGEVGVVRQAPFPSRAS{c-amid-C}	104%
17	17	{n-acet-{d β D}}{dS}{dY}GEVGVVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}}	104%
18	18	{dD}SYGEVGVVRQAPF{dP}SRASC	98%
19	19	{htt-cyclic-D}SYGEVGVVRQAPFPSRASC	103%
20	20	{n-peg12-{d β D}}{dS}{dY}GEVGVVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}}	104%
21	21	{n-peg40k-{d β D}}{dS}{dY}GEVGVVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}}	98%
22	22	{n-acet-{d β D}}{dS}{dY}GEVGVVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{r-peg40k-{dC}}}	102%
23	23	{n-acet-{d β D}}{dS}{dY}GEVGVVRQAPF{dP}{dS}{r-peg40k-dbcO}-{azide-K}{dA}{dS}{c-amid-{dC}}	103%
24	24	{n-acet-{d β D}}{dS}{dY}GEVGVVRQAPF{dP}{dS}{r-pal-K}{dA}{dS}{c-amid-{dC}}	108%
25	25	{n-acet-D}SYGEVGVVRQAPFPSKAS{c-amid-C}	100%
26	26	{n-acet-D}SYGEVGVVRQAPFPSKASC{c-amid-N}	103%
27	27	{n-acet-D}SYGEVGVVRQAPFPARASC{c-amid-N}	105%
28	28	{n-acet-D}SYGEVGVVRQAPFPSRVSC{c-amid-N}	99%
29	29	{n-acet-D}SYGEVGVVRQAPFPSRAAC{c-amid-N}	98%

SEQ ID NO:	PEP NO:	Amino acid sequence	% Activity at 100μM
30	30	{n-acet-D}SYGEVGVKQAPFPSRASC{c-amid-N}	97%
31	31	{n-acet-D}SYGEVGVRNAPFPSRASC{c-amid-N}	94%
32	32	{n-acet-D}SYGEVGVRQVPFPSRASC{c-amid-N}	89%
33	33	{n-acet-D}SYGEVGVRQAPFPARVSC{c-amid-N}	97%
34	34	{n-acet-D}SYGEVGVRQAPFPARVAC{c-amid-N}	97%
35	35	{n-acet-D}SYGEVGVKQAPFPARASC{c-amid-N}	97%
36	36	{n-acet-D}SYGEVGVKQAPFPARVAC{c-amid-N}	95%
37	37	{n-acet-D}SYGEVGVKQAPFPAKVA{c-amid-C}	101%
38	38	{n-acet-D}SYGEVGVRQAPFPS{dK}AS{c-amid-C}	99%
39	39	{n-acet-{dD}}SYGEVGVRQAPFPS{dK}AS{c-amid-C}	101%
40	40	{n-acet-{dD}}SYGEVGVRQAPFPS{dK}AS{c-amid-{dC}}	100%
41	41	{n-acet-{dD}}SYGEVGVRQAPF{dP}S{dK}AS{c-amid-{dC}}	99%
42	42	{n-acet-{dD}}{dS}{DMT}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{dS}{c-amid-{dC}}	107%
43	43	YGEVGVRQAPFPSRASC	104%
44	44	GEVGVRQAPFPSRASC	97%
45	45	KSYGEVGVRQAPFPSRASC	98%
46	46	DKYGEVGVRQAPFPSRASC	99%
47	47	DSKGEVGVRQAPFPSRASC	98%
48	48	DSYGVGVVRQAPFPSRASC	98%
49	49	DSYGEVGKRQAPFPSRASC	89%
50	50	DSYGEVGVRQAKFPSRASC	63%
51	51	DSYGEVGVRQAPKPSRASC	98%
52	52	DSYGEVGVRQAPFKSRASC	98%
53	53	DSYGEVGVRQAPFPKRASC	101%
54	54	DSYGEVGVRQAPFPKASC	101%
55	55	DSYGEVGVRQAPFPSRKASC	102%
56	56	DSYGEVGVRQAPFPSRAKASC	102%
57	57	DSYGEVGVRQAPFPSRASK	101%
58	58	SYGEVGVRQAPFPSRASC	103%
59	59	DYGEVGVRQAPFPSRASC	103%
60	60	DSGEVGVRQAPFPSRASC	103%
61	61	DSYEVGVVRQAPFPSRASC	101%
62	62	DSYGVGVVRQAPFPSRASC	102%
63	63	DSYGEVGVRQAPFPSRASC	79%
64	64	DSYGEVGVRQAPFPSRASC	99%
65	65	DSYGEVGVRQAPFPSRASC	103%
66	66	DSYGEVGVRQAPFPRASC	104%
67	67	DSYGEVGVRQAPFPSASC	102%
68	68	DSYGEVGVRQAPFPSRASC	102%
69	69	DSYGEVGVRQAPFPSRASC	102%
70	70	DSYGEVGVRQAPFPSRAS	99%
71	71	DWFGGEVGVRQAPFPLSISCN	102%
72	72	GEVGVRQAPFPLSISC	83%
73	73	GEVGVRQAPC	78%
74	74	WGIWGRQAPFPLSISCN	102%
75	75	WGIWGRQAPFPLSCN	105%
76	76	GEVGVRQAPFPSISC	97%
77	77	GEVGVRQAPFPLISC	96%
78	78	GEVGVRQAPFPISC	98%
79	79	DSYGEVGVRQAPYVPSISCN	102%
80	80	DSYGEVGVRQAPFPLQDCN	100%
81	81	GEVGVRQAPFPLSC	85%
82	82	SCDSYGEVGVRQAPFPSRA	101%
83	83	SRASCDSYGEVGVRQAPFP	111%
84	84	RQAPFPSRASCDSYGEVGV	53%
85	85	GEVGVRQAPFPSRASCDSY	105%
86	86	{n-acet-D}SYGEVGVRQAPFPS{r-pal-K}AS{c-amid-C}	115%
87	87	{n-acet-{dD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-ste-K}{dA}{dS}{c-amid-{dC}}	103%
88	88	DGEVGVRQAPFPSRASC	97%
89	89	AGEVGVRQAPFPSRASC	95%
90	90	WGEVGVRQAPFPSRASC	99%
91	91	GGEVGVRQAPFPSRASC	93%
92	92	DSYGEVGVRQAPFPSRASC	98%
93	93	DSYSEVGVRQAPFPSRASC	98%
94	94	DSYDEVGVVRQAPFPSRASC	94%
95	95	DSYAEVGVRQAPFPSRASC	91%
96	96	DSYGQVGVRQAPFPSRASC	101%
97	97	DSYGDVGVRQAPFPSRASC	103%
98	98	DSYGAVGVVRQAPFPSRASC	87%
99	99	DSYGEIGVRQAPFPSRASC	99%
100	100	DSYGELGVVRQAPFPSRASC	98%

SEQ ID NO:	PEP NO:	Amino acid sequence	% Activity at 100μM
101	101	DSYGEMGVRQAPFPSRASC	96%
102	102	DSYGEAGVRQAPFPSRASC	71%
103	103	DSYGEVSVRQAPFPSRASC	93%
104	104	DSYGEVAVRQAPFPSRASC	90%
105	105	DSYGEVGIRQAPFPSRASC	101%
106	106	DSYGEVGLRQAPFPSRASC	92%
107	107	DSYGEVGARQAPFPSRASC	100%
108	108	DSYGEVGVHQAAPFPSRASC	71%
109	109	DSYGEVGVRHAAAPFPSRASC	100%
110	110	DSYGEVGVREAAAPFPSRASC	62%
111	111	DSYGEVGVRAAPFPSRASC	88%
112	112	DSYGEVGVRRQAPFPSRASC	99%
113	113	DSYGEVGVRRTPFPSRASC	99%
114	114	DSYGEVGVRRQLPFPSRASC	63%
115	115	DSYGEVGVRRQASFPFPSRASC	95%
116	116	DSYGEVGVRRQAAPFPSRASC	86%
117	117	DSYGEVGVRRQAAPFPSRASC	106%
118	118	DSYGEVGVRRQAAPFPSRASC	102%
119	119	DSYGEVGVRRQAAPFPSRASC	101%
120	120	DSYGEVGVRRQAAPFPSRASC	101%
121	121	DSYGEVGVRRQAAPFPSRASC	98%
122	122	DSYGEVGVRRQAAPFPSRASC	98%
123	123	DSYGEVGVRRQAAPFPSRASC	100%
124	124	DSYGEVGVRRQAAPFPSRASC	99%
125	125	DSYGEVGVRRQAAPFPSRASC	100%
126	126	DSYGEVGVRRQAAPFPSRASC	101%
127	127	DSYGEVGVRRQAAPFPSRASC	101%
128	128	DSYGEVGVRRQAAPFPSRASC	102%
129	129	DSYGEVGVRRQAAPFPSRASC	100%
130	130	DSYGEVGVRRQAAPFPSRASC	99%
131	131	DSYGEVGVRRQAAPFPSRASC	101%
132	132	DSYGEVGVRRQAAPFPSRASC	96%
133	133	DSYGEVGVRRQAAPFPSRASC	99%
134	134	DSYGEVGVRRQAAPFPSRASC	102%
135	135	DSYGEVGVRRQAAPFPSRASC	100%
136	136	DSYGEVGVRRQAAPFPSRASC	89%
137	137	DSYGEVGVRRQAAPFPSRASC	96%
138	138	DSYGEVGVRRQAAPFPSRASC	100%
139	139	KKYGEVGVRRQAAPFPSRASC	99%
140	140	DYGEVGVRRQAAPFPSRASC	100%
141	141	DSYGEVGVRRQAAPFPSRASC	97%
142	142	DSYG{dE}VGVRRQAAPFPSRASC	96%
143	143	DSYGEVG{dV}RQAAPFPSRASC	87%
144	144	DSYGEVGVRRQAAPFPSRASC	85%
145	145	DSYG{βE}VGVRRQAAPFPSRASC	99%
146	146	DSYGEVGVRRQAAPFPSRASC	100%
147	147	DSYGEVGV{hR}QAAPFPSRASC	100%
148	148	DSYGEVGVRRQAAPFPSRASC	98%
149	149	DSYGEVGVRRQAAPFPSRASC	100%
150	150	DSYG{βhE}VGVRRQAAPFPSRASC	100%
151	151	DSYGE{βhV}GVRRQAAPFPSRASC	56%
152	152	DSYGEVG{βhV}RQAAPFPSRASC	91%
153	153	DSYGEVGVRRQAAPFPSRASC	75%
154	154	DSYGEVGVRRQAAPFPSRASC	91%
155	155	DSYGEVGVRRQAAPFPSRASC	98%
156	156	DSYGEVGVRRQAAPFPSRASC	101%
157	157	{n-acet-{dβD}}{dS}{dY}GEVGVRRQAAPF{dP}{dS}{r-pal-K}{dA}{c-amid-{dS}}	106%
158	158	{n-acet-D}SYGEVGVRRQAAPFPSRASC{c-amid-R}	77%
159	159	{n-acet-R}RDSYGEVGVRRQAAPFPSRAS{c-amid-C}	61%
160	160	{n-acet-D}SYGEVGVRRQAAPFPSRASCRRR{c-amid-R}	103%
161	161	{n-acet-R}RRRDSYGEVGVRRQAAPFPSRAS{c-amid-C}	59%
162	162	{n-acet-D}SYGEVGVRRQAAPFPSRA{c-amid-S}	100%
163	163	{n-acet-Y}GEVGVRRQAAPF{c-amid-P}	99%
164	164	{n-acet-Y}GEVGVRRQAAPFPSRA{c-amid-S}	98%
165	165	{n-acet-D}SYGEVGVRRQAAPF{c-amid-P}	98%
166	166	{n-acet-Y}GEVGVRRQAAPFPS{c-amid-R}	94%
167	167	{n-acet-Y}GEVGVRRQA{c-amid-P}	91%
168	168	{n-acet-{dβD}}{dS}{dY}GEVGVRRQAAPF{dP}{dS}{dR}{dA}{c-amid-{dS}}	97%
169	169	{n-pal-G}EVGVRRQA{c-amid-P}	100%
170	170	{n-pal-E}VGVRRQA{c-amid-P}	99%
171	171	{n-pal-V}GVRRQA{c-amid-P}	53%
172	172	{n-pal-Y}GEVGVRRQA{c-amid-A}	93%

SEQ ID NO:	PEP NO:	Amino acid sequence	% Activity at 100μM
173	173	{n-pal-Y}GEVGVVQA{c-amid-P}	103%
174	174	{n-pal-{dY}}GEVGVVQA{c-amid-P}	98%
175	175	{n-pal-Y}GEVGV{hR}QA{c-amid-P}	97%
176	176	{n-pal-Y}GEVGVVRA{c-amid-P}	100%
177	177	{n-pal-{dY}}GEVGV{hR}QA{c-amid-P}	97%
178	178	{n-pal-{dY}}GEVGVVRA{c-amid-P}	94%
179	179	{n-pal-Y}GEVGV{hR}HA{c-amid-P}	98%
180	180	{n-pal-D}SYGEVGVVQAFFPSRA{c-amid-S}	97%
181	181	{n-pal-G}LMGVVQAFFPLSISC{c-amid-N}	93%
182	182	{n-pal-G}LMGVVQA{c-amid-P}	88%
183	183	{n-acet-{dD}}{dS}{dY}GEVGVVQAFF{dP}{dS}{r-pal-K}{c-amid-{dA}}	112%
184	184	{n-acet-{dS}}{dY}GEVGVVQAFF{dP}S{c-amid-{r-pal-K}}	108%
185	185	{n-acet-Y}GEVGVVQAFFPS{c-amid-{r-pal-K}}	100%
186	186	{n-pal-D}SYGEVGVVQAFFPSRA{c-amid-S}	107%
187	187	{n-acet-D}SYGEVGVVQAFFPS{r-pal-K}A{c-amid-S}	108%
188	188	{n-pal-D}SYGEVGVVQAFFPS{r-pal-K}A{c-amid-S}	99%
189	189	{n-pal-Y}GEVGVVQAFF{c-amid-P}	109%
190	190	{n-acet-Y}GEVGVVQAFF{c-amid-F}	105%
191	191	{n-pal-Y}GEVGVVQAFF{c-amid-F}	103%
192	192	DSYGEVDVQAFFPS{r-pal-K}ASC	107%
193	193	{n-pal-G}EVGVVQA	101%
194	194	{n-pal-E}VGVVQA	98%
195	195	{n-pal-V}GVVQA	92%
196	196	{n-pal-G}VVQA	97%
197	197	{n-pal-V}VQA	96%
198	198	{n-pal-R}QAP	101%
	199	{n-pal-Q}AP	65%
200	200	{n-pal-G}EVGVVQA	102%
201	201	{n-pal-G}EVGVVQ	100%
202	202	{n-pal-G}EVGVV	107%
203	203	{n-pal-V}GVVQA	98%
204	204	{n-pal-V}GVV	61%
205	205	{n-pal-G}VVQA	89%
206	206	{n-pal-G}VVQA	82%
	207	{n-pal-G}VV	86%
208	208	{n-pal-D}SYEVGVVQAFFPSRAS	103%
209	209	{n-pal-D}SYGVGVVQAFFPSRAS	99%
210	210	{n-pal-D}SYGEVGVVQAFFPSRAS	63%
211	211	{n-pal-D}SYGEVGVVQAFFPSRAS	54%
212	212	{n-pal-D}SYGEVGVVQAFFPSRAS	62%
213	213	{n-pal-D}SYGEVGVVQAFFPSRAS	84%
214	214	{n-pal-D}SYGEVGVVQAFFPSRAS	97%
215	215	{n-pal-D}SYGVGVVQAFFPSRAS	94%
216	216	{n-pal-D}SYGVGVVQAFFPSRAS	85%
217	217	{n-pal-D}SYGEVQAFFPSRAS	63%
218	218	{n-pal-D}SYGEVQAFFPSRAS	67%
219	219	{n-pal-D}SYGEVQAFFPSRAS	60%
220	220	{n-pal-D}SYGEVGVVQAFFPSRAS	103%
221	221	{n-pal-D}SYGEVGVVQAFFPSRAS	102%
222	222	{n-pal-D}SYGEVGVVQAFFPSRAS	103%
223	223	{n-pal-D}SYGVVQAFFPSRAS	104%
224	224	{n-pal-D}SYGVVQAFFPSRAS	104%
225	225	{n-pal-D}SYGERQAFFPSRAS	61%
226	226	{n-pal-D}SYGEVQAFFPSRAS	73%
227	227	{n-pal-D}SYGEVQAFFPSRAS	72%
228	228	{n-pal-D}SYGEVGVVQAFFPSRAS	80%
229	229	{n-pal-D}SYGEVGVVQAFFPSRAS	69%
230	230	{n-pal-D}SYGEVGVVQAFFPSRAS	86%
231	231	{n-pal-D}SYGEVGVVQAFFPSRAS	103%
232	232	{n-pal-E}VGVVQA{c-amid-P}	104%
233	233	{n-pal-D}EVGVVQA{c-amid-P}	105%
234	234	{n-pal-E}VGVVQA{c-amid-R}	103%
235	235	{n-pal-D}EVGVVQA{c-amid-R}	104%
236	236	{n-pal-V}GVVQA{c-amid-P}	79%
237	237	{n-pal-E}GVVQA{c-amid-P}	91%
238	238	{n-pal-E}VVRQA{c-amid-P}	75%
239	239	{n-pal-E}VGVQA{c-amid-P}	95%
240	240	{n-pal-E}VGVRA{c-amid-P}	107%
241	241	{n-pal-E}VGVVQ{c-amid-P}	107%
242	242	{n-pal-E}VGVVQ{c-amid-A}	100%
243	243	{n-pal-A}VGVVQA{c-amid-P}	104%
244	244	{n-pal-E}AGVVQA{c-amid-P}	112%

SEQ ID NO:	PEP NO:	Amino acid sequence	% Activity at 100μM
245	245	{n-pal-E}VAVRQA{c-amid-P}	107%
246	246	{n-pal-E}VGARQA{c-amid-P}	106%
247	247	{n-pal-E}VGVAQA{c-amid-P}	70%
248	248	{n-pal-E}VGVRAA{c-amid-P}	112%
249	249	{n-pal-E}VGVRQG{c-amid-P}	101%
250	250	{n-pal-E}VGVRQA{c-amid-A}	98%
251	251	{n-pal-G}EVGVR	120%
252	252	{n-pal-V}RQAP	113%
253	253	{n-pal-G}EVGVR	123%
254	254	{n-pal-E}GVGVR	103%
255	255	{n-pal-G}VEGVR	89%
256	256	{n-pal-G}EGVVR	74%
257	257	{n-pal-G}EVGVK	120%
258	258	{n-pal-G}EVGVD	73%
259	259	{n-pal-G}EVGVE	92%
260	260	{n-pal-G}EVGVW	110%
261	261	{n-pal-G}EVGVA	113%
262	262	{n-pal-G}EVGVY	63%
263	263	{n-pal-G}EVGVC	96%
264	264	{n-pal-G}EVGAR	92%
265	265	{n-pal-G}EVGIR	105%
266	266	{n-pal-G}EVGTR	83%
267	267	{n-pal-G}EVGLR	101%
268	268	{n-pal-G}EVGWR	99%
269	269	{n-pal-G}EVGCR	96%
270	270	{n-pal-G}EVGFR	100%
271	271	{n-pal-G}EVGQR	85%
272	272	{n-pal-V}RQAP	98%
273	273	{n-pal-R}VQAP	106%
274	274	{n-pal-V}QRAP	74%
275	275	{n-pal-V}RAQP	107%
276	276	{n-pal-V}RQPA	98%
277	277	{n-pal-V}KQAP	60%
278	278	{n-pal-V}AQAP	63%
279	279	{n-pal-V}GQAP	78%
280	280	{n-pal-V}PQAP	98%
281	281	{n-pal-A}RQAP	98%
282	282	{n-pal-I}RQAP	102%
283	283	{n-pal-T}RQAP	103%
284	284	{n-pal-L}RQAP	105%
285	285	{n-pal-W}RQAP	100%
286	286	{n-pal-C}RQAP	101%
287	287	{n-pal-F}RQAP	66%
288	288	{n-pal-Q}RQAP	80%
289	289	{n-pal-H}RQAP	81%
290	290	{n-pal-P}RQAP	98%
291	291	DSYGEVGVVRQAPFPSKAS	102%
292	292	DSYGEVGVVRQAPFPSAAS	111%
293	293	DSYGEVGVVRQAPFPSNAS	109%
294	294	DSYGEVGVVRQAPFPSDAS	114%
295	295	DSYGEVGVVRQAPFPSCAS	111%
296	296	DSYGEVGVVRQAPFPSHAS	113%
297	297	DSYGEVGVVRQAPFPSYAS	114%
298	298	DSYKEVGVVRQAPFPSKAS	97%
299	299	DSYAEVGVVRQAPFPSKAS	91%
300	300	DSYNEVGVVRQAPFPSKAS	101%
301	301	DSYDEVGVVRQAPFPSKAS	95%
302	302	DSYCEVGVVRQAPFPSKAS	118%
303	303	DSYHEVGVVRQAPFPSKAS	96%
304	304	DSYYEVGVVRQAPFPSKAS	106%
305	305	{n-pal-S}ARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}YSD	93%
306	306	{n-pal-F}PAQRVGVEGYSD	65%
307	307	{n-pal-S}PFPAQRVGVEGYSD	71%
308	308	{n-pal-S}ARSPFAQRVGVEG	69%
309	309	{n-pal-S}ARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}	89%
310	310	{n-pal-{dP}}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}	52%
311	311	{n-pal-{dP}}{dA}{dQ}{dR}{dV}{dG}{dV}	90%
312	312	{n-pal-{dP}}{dA}{dQ}{dR}{dV}{dG}	76%
313	313	{n-pal-{dA}}{dQ}{dR}{dV}	62%
314	314	{n-pal-{dQ}}{dR}{dV}{dG}{dV}{dE}{dG}	104%
315	315	{n-pal-{dR}}{dV}{dG}{dV}{dE}{dG}	116%

Several of the peptides in Table 3, and described elsewhere in this patent disclosure, contain chemical modifications and/or contain “modified” amino acids. In Table 3, and elsewhere in this patent disclosure, amino acids and amino acid modifications are represented as follows.

Amino acids are represented using their single-letter amino acid code using capital letters.

- 5 Amino acids illustrated using capital letters unadorned with prefixes or surrounding braces are naturally occurring amino acids.

Modified amino acids are illustrated by enclosure with braces (“{” and “}”) which enclose the modification(s) to the amino acid residue. For example, {mod-A} or {modA} denotes a modified version of the naturally occurring alanine (A) amino acid residue according to an example
10 modification (mod or mod-). Specific modifications are represented using prefixes. For example, the amino acid modifications present in the peptides shown in Table 3 are represented using the following prefixes:

- D chirality of an amino acid is represented by the prefix “d”, e.g., {dD} denotes D-aspartic acid.
- 15 • Beta amino acids are represented by the prefix “β”, e.g., {βD} denotes beta aspartic acid.
- Homo amino acids are represented by the prefix “h”, e.g., {hD} denotes homo aspartic acid.
- Acetylation is represented by the prefix “acet-”.
- Amidation is represented by the prefix “amid-”.
- 20 • Palmitoylation is represented by the prefix “pal-”.
- Stearic acid conjugation is represented by the prefix “ste-”.
- Polyethylene glycol (PEG) conjugation is represented by the prefix “peg-”. The number (#) of repeating ethylene glycol units in a conjugated PEG moiety may be represented using the prefix “peg#-” e.g., the prefix “peg12-” represents conjugation of a
25 polyethylene glycol moiety consisting of 12 ethylene glycol units. The molecular weight of a PEG moiety may also be represented, e.g., the prefix “peg40k-” represents conjugation of a PEG moiety having a molecular weight of 40 kDa.

Several of the peptides in Table 3, and described elsewhere in this patent disclosure, are cyclized. In Table 3, and elsewhere in this patent disclosure, cyclization of a peptide is
30 represented by the prefix “cyclic-”. “Head-to-tail” cyclization of a peptide (i.e., N-terminal cyclization of a peptide to its C-terminus) is represented by the prefix “htt-cyclic-”.

Several of the peptides in Table 3, and described elsewhere in this patent disclosure, include the amino acid surrogate N,N-Dimethyltryptamine. In Table 3, and elsewhere in this patent disclosure, the abbreviation “DMT” refers to N,N-Dimethyltryptamine.

In Table 3, and elsewhere in this patent disclosure, the locations of amino acid modifications may also be represented. For example, modifications to an N-terminus, R side chain, or C-terminus may be presented with “n-”, “r-”, or “c-” prefixes, respectively, for example, N-terminal acetylation is represented by the prefix “n-acet-”, N-terminal palmitoylation is represented by the prefix “n-pal-”, side chain palmitoylation is represented by the prefix “r-pal-” (for example palmitoylation of a lysine side chain is represented as {r-pal-K}), N-terminal conjugation of polyethylene glycol (PEG) is represented by the prefix “n-peg-” (for example N-terminal conjugation of polyethylene glycol to D-cysteine is represented as {n-peg-{dC}} and N-terminal conjugation of a polyethylene glycol (PEG) moiety having 12 ethylene glycol monomers to D-beta aspartic acid is represented as {n-peg12-{dβD}}), and N-terminal conjugation of a 40 kDa average molecular weight PEG moiety is represented as “n-peg40k-”), side chain conjugation of stearic acid is represented by the prefix “r-ste-” (for example conjugation of stearic acid to a lysine side chain is represented as {r-ste-K}), side chain conjugation of polyethylene glycol (PEG) is represented by the prefix “r-peg-” (for example side chain conjugation of polyethylene glycol to D-cysteine is represented as {r-peg-{dC}} and, side chain conjugation of a polyethylene glycol (PEG) moiety having 12 ethylene glycol monomers to D-cysteine is represented as {r-peg12-{dC}}), and side chain conjugation of a 40 kDa average molecular weight PEG moiety is represented as “r-peg40k-”), and C-terminal amidation is represented by the prefix “c-amid-”. In Table 3, and elsewhere in this patent disclosure, combinations of any of the prefixes described above are used where necessary to appropriately represent amino acid modifications or other peptide attributes. For example, the combination of prefixes {n-acet-{dβD}} represents an N-terminal D-beta aspartic acid amino acid residue that has an acetyl group attached to its free N-terminal amino group. In Table 3, and elsewhere in this patent disclosure, the conjugation of PEG40k with lysine using the reaction of PEG40k-DBCO with lysine-azide is represented as {{r-peg40k-dbco}-{azide-K}}. In Table 3, and elsewhere in this patent disclosure, the conjugation of PEG40k with cysteine using the reaction of PEG40k-Maleimide with cysteine is represented as {r-peg40k-C}. In Table 3, and elsewhere in this patent disclosure, the conjugation of PEG40k with D-cysteine using the reaction of PEG40k-Maleimide with cysteine is represented as {r-peg40k-{dC}}.

In one embodiment, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 1. In one embodiment, the present invention provides a peptide

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In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 3. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 4. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 5. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 6. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 7. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 8. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 9. In one embodiment,

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invention provides a peptide having the chemical structure shown in Fig. 41. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 42. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 43. In one embodiment, the present invention provides a peptide having the chemical structure shown in Fig. 44.

2.2. Activity Groups

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1-315. Such peptides exhibit DOR agonist activity of at least 50% at or below 100 μ M as described in Example 1.

10 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 15 95, 96, 97, 98, 99, 100, 101, 103, 104, 105, 106, 107, 109, 111, 112, 113, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 152, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 20 198, 200, 201, 202, 203, 205, 206, 207, 208, 209, 213, 214, 215, 216, 220, 221, 222, 223, 224, 228, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 248, 249, 250, 251, 252, 253, 254, 255, 257, 259, 260, 261, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 275, 276, 279, 280, 281, 282, 283, 284, 285, 286, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, or 304. Such peptides form a group of peptides 25 (“Group 1”) and, along with PEP NOs: and/or SEQ ID NOs: 305, 309, 311, 312, 314, and 315, form a group of peptides (“Group 1A”). The peptides of both Group 1 and Group 1A exhibit DOR agonist activity of at least 75% at or below 100 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 30 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 74, 75, 76, 77, 78, 79, 80, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 99, 100, 101, 103, 104, 105, 106, 107, 109, 112, 113, 115, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 137, 138, 139, 140, 141, 142, 145, 146, 147,

148, 149, 150, 152, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 200, 201, 202, 203, 208, 209, 214, 215, 220, 221, 222, 223, 224, 231, 232, 233, 234, 235, 237, 239, 240, 241, 242, 243, 244, 245, 246, 248, 249, 5 250, 251, 252, 253, 254, 257, 259, 260, 261, 263, 264, 265, 267, 268, 269, 270, 272, 273, 275, 276, 280, 281, 282, 283, 284, 285, 286, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, and 304. Such peptides form a group of peptides ("Group 2") and, along with PEP NOs: and/or SEQ ID NOs: 305, 309, 314, and 315, form a group of peptides ("Group 2A"). The peptides of both Group 2 and Group 2A exhibit DOR agonist activity of at least 90% at or below 10 100 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 15 70, 71, 74, 75, 76, 77, 78, 79, 80, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 95, 96, 97, 99, 100, 101, 103, 105, 107, 109, 112, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 137, 138, 139, 140, 141, 142, 145, 146, 147, 148, 149, 150, 152, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 20 194, 195, 196, 197, 200, 201, 202, 203, 205, 206, 207, 208, 209, 213, 214, 215, 216, 223, 224, 228, 230, 231, 232, 233, 234, 235, 236, 237, 239, 240, 241, 242, 243, 244, 245, 246, 248, 249, 250, 251, 252, 253, 254, 255, 257, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 275, 276, 280, 281, 282, 283, 284, 285, 286, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 301, 302, 303, and 304. Such peptides form a group of peptides ("Group 3") and, along with PEP NOs: 25 and/or SEQ ID NOs: 305, 309, 311, and 315, form a group of peptides ("Group 3A"). The peptides of both Group 3 and Group 3A exhibit DOR agonist activity of at least 50% at or below 10 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 30 15, 16, 17, 18, 19, 20, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 45, 46, 47, 48, 52, 53, 54, 55, 56, 57, 58, 59, 60, 62, 64, 65, 66, 67, 68, 69, 70, 71, 74, 75, 78, 79, 80, 82, 83, 86, 87, 88, 89, 90, 92, 96, 97, 99, 100, 105, 107, 109, 112, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 128, 129, 130, 131, 134, 135, 137, 138, 139, 140, 145, 146, 147, 148, 149, 150, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 169, 170, 173,

174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 200, 201, 202, 203, 205, 208, 209, 214, 215, 223, 224, 231, 232, 233, 234, 235, 237, 240, 241, 242, 243, 244, 245, 246, 248, 249, 250, 251, 252, 253, 254, 255, 257, 264, 265, 266, 268, 270, 272, 273, 281, 282, 283, 284, 286, 288, 289, 290, 291, 292, 293, 294, 5 295, 296, 297, and 304. Such peptides form a group of peptides ("Group 4") and, along with PEP NOs: and/or SEQ ID NOs: 305, and 309, form a group of peptides ("Group 4A"). The peptides of both Group 4 and Group 4A exhibit DOR agonist activity of at least 75% at or below 10 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid
10 sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 20, 22, 23, 24, 25, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 42, 43, 45, 46, 52, 53, 54, 55, 56, 57, 58, 59, 60, 65, 66, 67, 68, 69, 70, 71, 75, 79, 80, 82, 83, 86, 87, 90, 92, 96, 97, 99, 109, 112, 117, 118, 119, 120, 123, 124, 125, 126, 128, 129, 130, 131, 134, 135, 138, 139, 140, 145, 147, 149, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 169, 170, 173, 174,
15 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 196, 197, 200, 201, 202, 208, 209, 214, 215, 223, 224, 231, 232, 233, 234, 235, 237, 240, 241, 242, 243, 244, 245, 246, 248, 249, 250, 251, 252, 253, 254, 257, 265, 268, 272, 282, 284, 286, 290, 291, 292, 293, 295, 296, and 297. Such peptides form a group of peptides ("Group 5") and, along with PEP NO: and/or SEQ ID NO: 309, form a group of peptides ("Group 5A"). The peptides of both
20 Group 5 and Group 5A exhibit DOR agonist activity of at least 90% at or below 10 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid
sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 13, 14,
15 15, 16, 17, 19, 20, 22, 23, 24, 25, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 42, 43, 45, 46, 52, 53, 54, 55, 56, 57, 58, 59, 60, 62, 65, 66, 67, 68, 69, 70, 71, 74, 75, 79, 80, 82, 83, 85, 86, 87,
25 90, 92, 96, 97, 99, 105, 107, 109, 112, 117, 118, 119, 120, 125, 126, 128, 129, 130, 131, 134, 138, 139, 140, 147, 149, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 169, 170, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 200, 201, 202, 205, 208, 209, 214, 215, 223, 224, 231, 232, 233,
30 234, 235, 237, 240, 241, 242, 243, 244, 245, 246, 248, 249, 250, 251, 252, 253, 254, 257, 265, 268, 270, 272, 282, 284, 285, 286, 288, 289, 290, 292, 293, 296, and 297. Such peptides form a group of peptides ("Group 6") and, along with PEP NOs: and/or SEQ ID NOs: 305, and 309, form a group of peptides ("Group 6A"). The peptides of both Group 6 and Group 6A exhibit DOR agonist activity of at least 50% at or below 1 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 7, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 20, 22, 24, 25, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 42, 43, 45, 46, 52, 53, 54, 55, 56, 57, 58, 59, 60, 65, 66, 67, 68, 69, 70, 71, 75, 79, 82, 83, 86, 87, 90, 92, 96, 99, 109, 117, 118, 119, 125, 126, 129, 130, 131, 139, 140, 147, 149, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 169, 170, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 200, 201, 202, 205, 208, 209, 214, 215, 223, 224, 232, 233, 234, 235, 237, 240, 241, 242, 243, 244, 245, 246, 248, 249, 250, 252, 254, 257, 268, 272, 282, 284, and 290. Such peptides form a group of peptides ("Group 7") and, along with PEP NOs: and/or SEQ ID NOs: 305, and 309, form a group of peptides ("Group 7A"). The peptides of both Group 7 and Group 7A exhibit DOR agonist activity of at least 75% at or below 1 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 7, 10, 11, 12, 15, 16, 17, 24, 25, 26, 27, 28, 29, 33, 35, 36, 37, 38, 42, 43, 45, 46, 53, 54, 55, 56, 57, 58, 59, 60, 65, 66, 67, 68, 69, 70, 71, 79, 82, 83, 86, 87, 92, 109, 117, 119, 126, 131, 139, 140, 147, 149, 156, 157, 158, 159, 160, 161, 162, 163, 169, 170, 173, 174, 176, 178, 180, 183, 184, 185, 186, 187, 188, 189, 191, 193, 194, 200, 201, 202, 208, 209, 214, 215, 232, 233, 234, 235, 241, 242, 243, 244, 245, 246, 248, 249, 250, 252, 272, 282, and 284. Such peptides form a group of peptides ("Group 8") and, along with PEP NO: and/or SEQ ID NO: 309, form a group of peptides ("Group 8A"). The peptides of both Group 8 and Group 8A exhibit DOR agonist activity of at least 90% at or below 1 μ M as described in Example 1.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 16, 17, 24, 86, 87, 157, 162, 163, 164, 165, 166, 167, 170, 171, 173, 175, 177, 178, 179, 182, 183, 185, 186, or 187. Such peptides were demonstrated to have an analgesic effect in vivo, as described in Example 5. Such peptides form a group of peptides ("Group 9").

2.3. Modification Groups

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137,

138, 139, 140, 141, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain only naturally occurring amino acids and can be produced synthetically or using non-synthetic methods (such as by expression of a nucleotide sequence that encodes the peptide in a suitable cell type). Such peptides form a group of peptides ("Group 10").

5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 11, 16, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 169, 170, 171, 172, 173, 176, 180, 181, 182, 186, 189, 190, 191, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223,
10 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 306, 307, 308. Such peptides contain only N-terminal or C-terminal modifications and naturally occurring amino acids and can be produced
15 synthetically or using a combination of non-synthetic methods (such as by expression of a nucleotide sequence that encodes the peptide in a suitable cell type) and chemical modification. Such peptides form a group of peptides ("Group 11").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 24, 42, 86, 87, 157, 169, 170, 171, 172,
20 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268,
25 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315. Such peptides contain a fatty acid and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides ("Group 12").

In some embodiments, the present invention provides a peptide comprising the amino acid
30 sequence of any one of PEP NOs: and/or SEQ ID NOs: 24, 42, 86, 157, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250,

251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315. Such peptides contain a palmitic acid and may exhibit improved properties such as affinity, specificity, and
5 pharmacokinetic properties. Such peptides form a group of peptides (“Group 13”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 186, 188, 189, 191, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220,
10 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315. Such peptides contain an N-terminal palmitic acid and may exhibit
15 improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 14”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 24, 42, 86, 157, 183, 184, 185, 187, 188, 192. Such peptides contain a palmitoylated lysine and may exhibit improved properties such as
20 affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 15”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 20, 21, 22, 23. Such peptides contain a polyethylene glycol and may exhibit improved properties such as affinity, specificity, and
25 pharmacokinetic properties. Such peptides form a group of peptides (“Group 16”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 86, 87, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162,
30 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 252, 253, 254, 255, 256, 257,

258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 305, 306, 307, 308, 309, 310, 311, 312, 313, 314, 315. Such peptides contain non-naturally occurring amino acids and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties.

5 Such peptides form a group of peptides (“Group 17”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 12, 13, 14, 15, 17, 18, 20, 21, 22, 23, 24, 38, 39, 40, 41, 42, 87, 142, 143, 144, 157, 168, 174, 177, 178, 183, 184, 305, 309, 310, 311, 312, 313, 314, 315. Such peptides contain a D-amino acid and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 18”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 175, 177, 179. Such peptides contain a homo amino acid and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 19”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 13, 17, 20, 21, 22, 23, 24, 42, 87, 145, 146, 150, 151, 152, 153, 154, 155, 156, 157, 168. Such peptides contain a beta amino acid and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 20”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 150, 151, 152, 153, 154, 155, 156. Such peptides contain a beta homo amino acid and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 21”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 13, 17, 20, 21, 22, 23, 24, 42, 87, 157, 168. Such peptides contain a D-beta aspartic acid and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides (“Group 22”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 16, 17, 22, 23, 24, 25, 26, 27, 28, 29, 30,

31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 86, 87, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 183, 184, 185, 187, 190. Such peptides have N-terminal acetylation and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides ("Group 23").

5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 11, 12, 16, 17, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 86, 87, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 232, 233, 234, 235, 236, 237, 238, 239, 240, 10 241, 242, 243, 244, 245, 246, 247, 248, 249, 250. Such peptides have C-terminal amidation and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides ("Group 24").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 19. Such peptides have a cyclic 15 conformation and may exhibit improved properties such as affinity, specificity, and pharmacokinetic properties. Such peptides form a group of peptides ("Group 25").

2.4. Sequence Groups

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 20 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 149, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 25 214, 221, 222, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 9 amino acid sequence GEVGVRQAP (PEP NO: and/or SEQ ID NO: 747). Such peptides form a group of peptides ("Group 26").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 30 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144,

148, 149, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 213, 214, 221, 222, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 8 amino acid sequence GEVGVRQA (PEP NO: and/or SEQ ID NO: 753). Such peptides form a group of peptides ("Group 27").

5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 112, 113, 114, 115, 116, 117, 118, 119, 120, 10 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 148, 149, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 172, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 212, 213, 214, 220, 221, 222, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 7 amino acid sequence GEVGVRQ (PEP NO: and/or SEQ ID NO: 751). Such peptides form a group of peptides ("Group 28"). 15

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 31, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 20 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 148, 149, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 172, 173, 174, 176, 178, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 212, 213, 214, 220, 221, 222, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. 25 Such peptides contain the 6 amino acid sequence GEVGVR (PEP NO: and/or SEQ ID NO: 752). Such peptides form a group of peptides ("Group 29").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 30 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 147, 148, 149, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 172, 173, 174, 175, 176, 177,

178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 211, 212, 213, 214, 220, 221, 222, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 5 amino acid sequence GEVGV (PEP NO: and/or SEQ ID NO: 754). Such peptides form a group of peptides (“Group 30”).

- 5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 211, 212, 213, 214, 219, 220, 221, 222, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297.
- 15 Such peptides contain the 4 amino acid sequence GEVG (PEP NO: and/or SEQ ID NO: 755). Such peptides form a group of peptides (“Group 31”).

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 211, 212, 213, 214, 217, 218, 219, 220, 221, 222, 226, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 3 amino acid sequence GEV (PEP NO: 756). Such peptides form a group of peptides (“Group 32”).
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- 25

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 149,
- 30

156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 208, 214, 221, 222, 231, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 8 amino acid sequence EVGVRQAP (PEP NO: and/or SEQ ID NO: 757). Such peptides form a group of peptides ("Group 33").

5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 115, 116, 117, 118, 119, 120, 10 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 148, 149, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 200, 208, 213, 214, 221, 222, 230, 231, 233, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 7 amino acid sequence EVGVRQA (PEP NO: and/or SEQ ID NO: 15 758). Such peptides form a group of peptides ("Group 34").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 20 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 148, 149, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 200, 201, 208, 212, 213, 214, 220, 221, 222, 229, 230, 231, 233, 235, 291, 292, 293, 294, 25 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 6 amino acid sequence EVGVRQ (PEP NO: and/or SEQ ID NO: 759). Such peptides form a group of peptides ("Group 35").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 30 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 31, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 148, 149, 153, 154, 155, 156, 157, 158,

159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174, 176, 178, 180, 183, 184,
185, 186, 187, 188, 189, 190, 191, 193, 200, 201, 202, 208, 212, 213, 214, 220, 221, 222, 229,
230, 231, 233, 235, 251, 253, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303,
304. Such peptides contain the 5 amino acid sequence EVGVR (PEP NO: and/or SEQ ID NO:
5 760). Such peptides form a group of peptides ("Group 36").

In some embodiments, the present invention provides a peptide comprising the amino acid
sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,
15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,
41, 42, 43, 44, 45, 46, 47, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68, 69,
10 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 108,
109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127,
128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 147, 148, 149,
153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173,
174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 200, 201,
15 202, 208, 211, 212, 213, 214, 220, 221, 222, 228, 229, 230, 231, 233, 235, 251, 253, 257, 258,
259, 260, 261, 262, 263, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304.
Such peptides contain the 4 amino acid sequence EVGV (PEP NO: and/or SEQ ID NO: 761).
Such peptides form a group of peptides ("Group 37").

In some embodiments, the present invention provides a peptide comprising the amino acid
20 sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,
15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,
41, 42, 43, 44, 45, 46, 47, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 63, 64, 65, 66, 67, 68,
69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95,
105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123,
25 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 143,
144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165,
166, 167, 168, 169, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188,
189, 190, 191, 193, 200, 201, 202, 208, 211, 212, 213, 214, 219, 220, 221, 222, 227, 228, 229,
230, 231, 233, 235, 251, 253, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269,
30 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides
contain the 3 amino acid sequence EVG (PEP NO: 762). Such peptides form a group of peptides
("Group 38").

In some embodiments, the present invention provides a peptide comprising the amino acid
sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,

- 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 149, 150, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 208, 209, 214, 215, 221, 222, 231, 234, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 7 amino acid sequence VGVRQAP (PEP NO: and/or SEQ ID NO: 748). Such peptides form a group of peptides ("Group 39").
- 10 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 148, 149, 150, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 200, 208, 209, 213, 214, 215, 221, 222, 230, 231, 232, 233, 234, 235, 243, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 6 amino acid sequence VGVRQA (PEP NO: and/or SEQ ID NO: 763). Such peptides form a group of peptides ("Group 40").
- 20

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 146, 148, 149, 150, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 200, 201, 208, 209, 212, 213, 214, 215, 220, 221, 222, 229, 230, 231, 232, 233, 234, 235, 241, 242, 243, 249, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 5 amino acid sequence VGVRQ (PEP NO: and/or SEQ ID NO: 764). Such peptides form a group of peptides ("Group 41").

30

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 31, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 5 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 146, 148, 149, 150, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 176, 178, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 200, 201, 10 202, 208, 209, 212, 213, 214, 215, 220, 221, 222, 229, 230, 231, 232, 233, 234, 235, 240, 241, 242, 243, 248, 249, 250, 251, 253, 254, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 4 amino acid sequence VGVR (PEP NO: and/or SEQ ID NO: 765). Such peptides form a group of peptides ("Group 42").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 20 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 146, 147, 148, 149, 150, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 200, 201, 202, 208, 209, 211, 212, 213, 214, 215, 220, 221, 222, 228, 229, 230, 231, 232, 233, 234, 235, 239, 240, 241, 242, 243, 247, 248, 249, 250, 251, 253, 25 254, 257, 258, 259, 260, 261, 262, 263, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 306, 307, 308. Such peptides contain the 3 amino acid sequence VGV (PEP NO: 766). Such peptides form a group of peptides ("Group 43").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 30 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 149, 150, 151, 156, 157, 158, 159, 160, 161, 162,

163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 195, 203, 208, 209, 210, 214, 215, 216, 221, 222, 223, 224, 231, 234, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 6 amino acid sequence GVRQAP (PEP NO: and/or SEQ ID NO: 749). Such peptides form a group of peptides
5 (“Group 44”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73,
10 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 148, 149, 150, 151, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 195, 200, 203, 208, 209, 210, 213, 214,
15 215, 216, 221, 222, 223, 224, 230, 231, 232, 233, 234, 235, 236, 237, 243, 244, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 5 amino acid sequence GVRQA (PEP NO: and/or SEQ ID NO: 767). Such peptides form a group of peptides (“Group 45”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128,
20 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 146, 148, 149, 150, 151, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 195, 200, 201, 203, 208, 209, 210, 212, 213, 214, 215, 216, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 235, 236, 237, 241, 242, 243, 244, 249, 250, 291, 292, 293, 294, 295, 296, 297,
25 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 4 amino acid sequence GVRQ (PEP NO: and/or SEQ ID NO: 768). Such peptides form a group of peptides (“Group 46”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 31, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44,

45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 146, 148, 149, 150, 151, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 176, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 193, 194, 195, 200, 201, 202, 203, 204, 208, 209, 210, 212, 213, 214, 215, 216, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 235, 236, 237, 240, 241, 242, 243, 244, 248, 249, 250, 251, 253, 254, 255, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence GVR (PEP NO: 769). Such peptides form a group of peptides ("Group 47").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 149, 150, 151, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 203, 205, 208, 209, 210, 214, 215, 216, 217, 218, 221, 222, 223, 224, 231, 234, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 5 amino acid sequence VRQAP (PEP NO: and/or SEQ ID NO: 770). Such peptides form a group of peptides ("Group 48").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 148, 149, 150, 151, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 203, 205, 206, 208, 209, 210, 213, 214, 215, 216, 217, 218, 221, 222, 223, 224, 230, 231, 232, 233, 234, 235, 236, 237, 238, 243, 244, 245, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301,

302, 303, 304. Such peptides contain the 4 amino acid sequence VRQA (PEP NO: and/or SEQ ID NO: 750). Such peptides form a group of peptides ("Group 49").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 144, 145, 146, 148, 149, 150, 151, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 201, 203, 205, 206, 208, 209, 210, 212, 213, 214, 215, 216, 217, 218, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 241, 242, 243, 244, 245, 249, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence VRQ (PEP NO: 771). Such peptides form a group of peptides ("Group 50").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 149, 150, 151, 152, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 203, 205, 208, 209, 210, 214, 215, 216, 217, 218, 221, 222, 223, 224, 225, 231, 234, 235, 252, 272, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 4 amino acid sequence RQAP (PEP NO: and/or SEQ ID NO: 772). Such peptides form a group of peptides ("Group 51").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98,

- 99, 100, 101, 102, 103, 104, 105, 106, 107, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 148, 149, 150, 151, 152, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 200, 203, 205, 206, 208, 209, 210, 213, 214, 215, 216, 217, 218, 221, 222, 223, 224, 225, 230, 231, 232, 233, 234, 235, 236, 237, 238, 243, 244, 245, 246, 250, 252, 272, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence RQA (PEP NO: 773). Such peptides form a group of peptides ("Group 52").
- 10 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 747 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 748 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 749 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 750 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 751 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 752 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 753 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 754 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 755 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 756 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 757 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 758 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino

acid sequence of PEP NO: and/or SEQ ID NO: 759 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 760 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 761 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 762 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 763 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 764 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 765 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 766 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 767 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 768 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 769 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 770 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 771 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 772 wherein the peptide has delta opioid agonist activity. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 773 wherein the peptide has delta opioid agonist activity.

2.5. Sequence Groups with Variants

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,

41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 208, 209, 210, 211, 212, 213, 214, 220, 221, 222, 229, 230, 231, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 26 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 53").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174, 175, 176, 177, 178, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 200, 208, 209, 210, 211, 212, 213, 214, 220, 221, 222, 229, 230, 231, 233, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 27 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 54").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174,

175, 176, 177, 178, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 200, 201, 208, 209, 210, 211, 212, 213, 214, 220, 221, 222, 229, 230, 231, 233, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 28 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 55").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 200, 201, 202, 208, 209, 210, 211, 212, 213, 214, 219, 220, 221, 222, 227, 228, 229, 230, 231, 233, 235, 251, 253, 254, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 29 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 56").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 200, 201, 202, 208, 209, 210, 211, 212, 213, 214, 219, 220, 221, 222, 227, 228, 229, 230, 231, 233, 235, 251, 253, 254, 257, 258, 259, 260, 261, 262, 263, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that

defines Group 30 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 57").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 200, 201, 202, 208, 209, 210, 211, 212, 213, 214, 217, 218, 219, 220, 221, 222, 226, 227, 228, 229, 230, 231, 233, 235, 251, 253, 254, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 31 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 58").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 239, 240, 241, 242, 243, 244, 247, 248, 249, 250, 251, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 314, 315. Such peptides contain a variant of the amino acid sequence that defines Group 32 in

which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 59").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 173, 174, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 200, 208, 209, 210, 211, 212, 213, 214, 215, 220, 221, 222, 229, 230, 231, 233, 234, 235, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 33 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 60").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 200, 201, 208, 209, 210, 211, 212, 213, 214, 215, 220, 221, 222, 229, 230, 231, 232, 233, 234, 235, 237, 243, 244, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 34 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 61").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,

41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66,
67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95,
96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115,
116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134,
5 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153,
154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173,
174, 175, 176, 177, 178, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 200,
201, 202, 208, 209, 210, 211, 212, 213, 214, 215, 220, 221, 222, 229, 230, 231, 232, 233, 234,
235, 237, 241, 242, 243, 244, 249, 250, 251, 253, 291, 292, 293, 294, 295, 296, 297, 298, 299,
10 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines
Group 35 in which one of the amino acids in the sequence is deleted or substituted with a
different amino acid. Such peptides form a group of peptides ("Group 62").

In some embodiments, the present invention provides a peptide comprising the amino acid
sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,
15 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,
41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66,
67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94,
95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114,
115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133,
20 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152,
153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172,
173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193,
194, 200, 201, 202, 208, 209, 210, 211, 212, 213, 214, 215, 219, 220, 221, 222, 227, 228, 229,
230, 231, 232, 233, 234, 235, 237, 240, 241, 242, 243, 244, 248, 249, 250, 251, 253, 254, 255,
25 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294,
295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino
acid sequence that defines Group 36 in which one of the amino acids in the sequence is deleted
or substituted with a different amino acid. Such peptides form a group of peptides ("Group 63").

In some embodiments, the present invention provides a peptide comprising the amino acid
30 sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14,
15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,
41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66,
67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94,
95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114,

115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 5 194, 200, 201, 202, 208, 209, 210, 211, 212, 213, 214, 215, 219, 220, 221, 222, 227, 228, 229, 230, 231, 232, 233, 234, 235, 237, 239, 240, 241, 242, 243, 244, 247, 248, 249, 250, 251, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 306, 307, 308. Such peptides contain a variant of the amino acid sequence that defines Group 37 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 64").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 15 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 20 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 172, 173, 174, 175, 176, 177, 178, 179, 180, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 200, 201, 202, 208, 209, 210, 211, 212, 213, 214, 215, 217, 218, 219, 220, 221, 222, 226, 227, 228, 229, 230, 231, 232, 233, 234, 235, 237, 239, 240, 241, 242, 243, 244, 246, 247, 248, 249, 250, 251, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 25 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 314, 315. Such peptides contain a variant of the amino acid sequence that defines Group 38 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 65").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115,

116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 173, 174, 180, 181, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 200, 203, 208, 209, 5 210, 211, 212, 213, 214, 215, 216, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 235, 241, 243, 249, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 39 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 66").

10 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 15 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 20 193, 194, 195, 200, 201, 203, 208, 209, 210, 211, 212, 213, 214, 215, 216, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 40 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides 25 form a group of peptides ("Group 67").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 30 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172,

173, 174, 175, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 200, 201, 202, 203, 208, 209, 210, 211, 212, 213, 214, 215, 216, 220, 221, 222, 223, 224, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 253, 254, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 41 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 68”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 200, 201, 202, 203, 204, 208, 209, 210, 211, 212, 213, 214, 215, 216, 219, 220, 221, 222, 223, 224, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 306, 307, 308. Such peptides contain a variant of the amino acid sequence that defines Group 42 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 69”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190,

191, 192, 193, 194, 195, 200, 201, 202, 203, 204, 208, 209, 210, 211, 212, 213, 214, 215, 216, 219, 220, 221, 222, 223, 224, 227, 228, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 5 298, 299, 300, 301, 302, 303, 304, 305, 306, 307, 308, 309, 310, 311, 314, 315. Such peptides contain a variant of the amino acid sequence that defines Group 43 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 70").

In some embodiments, the present invention provides a peptide comprising the amino acid
10 sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114,
15 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 203, 205, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 220, 221, 222, 223, 224,
20 225, 229, 230, 231, 232, 233, 234, 235, 236, 237, 241, 243, 244, 249, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 44 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 71").

In some embodiments, the present invention provides a peptide comprising the amino acid
25 sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114,
30 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 201, 203, 205, 206, 208, 209, 210, 211, 212, 213, 214, 215, 216,

217, 218, 220, 221, 222, 223, 224, 225, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 45 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 72”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 201, 202, 203, 204, 205, 206, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 220, 221, 222, 223, 224, 225, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 253, 254, 255, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 46 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 73”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230,

231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251, 253, 254, 255, 256, 257, 258, 259, 260, 261, 262, 263, 264, 265, 266, 267, 268, 269, 270, 271, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 306, 307, 308.

Such peptides contain a variant of the amino acid sequence that defines Group 47 in which one
5 of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 74").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,
10 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151,
15 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 200, 203, 205, 206, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 241, 243, 244, 245, 249, 250, 252, 272, 273, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289,
20 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 48 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides ("Group 75").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113,
25 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 200, 201, 203, 205, 206, 208, 209, 210, 211, 212, 213, 214,

215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 252, 272, 273, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid
5 sequence that defines Group 49 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 76”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40,
10 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151,
15 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 200, 201, 202, 203, 204, 205, 206, 207, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 251,
20 252, 253, 254, 255, 256, 271, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain a variant of the amino acid sequence that defines Group 50 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 77”).

25 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92,
30 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 173, 174, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195,

196, 197, 198, 200, 203, 205, 206, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 229, 230, 231, 232, 233, 234, 235, 236, 237, 238, 241, 243, 244, 245, 246, 249, 250, 252, 272, 273, 274, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304.

- 5 Such peptides contain a variant of the amino acid sequence that defines Group 51 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides form a group of peptides (“Group 78”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 10 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 15 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 200, 201, 203, 205, 206, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 20 232, 233, 234, 235, 236, 237, 238, 239, 240, 241, 242, 243, 244, 245, 246, 247, 248, 249, 250, 252, 272, 273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 305, 308, 309. Such peptides contain a variant of the amino acid sequence that defines Group 52 in which one of the amino acids in the sequence is deleted or substituted with a different amino acid. Such peptides 25 form a group of peptides (“Group 79”).

2.6. Additional Sequence Groups

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 14, 57, 70, 92, 159, 161. Such peptides contain the 18 amino acid sequence DSYGEVGVRQAPFPSRAS (PEP NO: 30 and/or SEQ ID NO: 70). Such peptides form a group of peptides (“Group 80”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 14, 56, 57, 69, 70, 82, 92, 126, 159, 161. Such peptides contain the 17 amino acid sequence

DSYGEVGVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 126). Such peptides form a group of peptides ("Group 81").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 14, 55, 56, 57, 68, 69,
5 70, 82, 92, 125, 126, 131, 159, 161. Such peptides contain the 16 amino acid sequence DSYGEVGVRQAPFPSR (PEP NO: and/or SEQ ID NO: 131). Such peptides form a group of peptides ("Group 82").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 14, 54, 55, 56, 57, 67,
10 68, 69, 70, 82, 92, 124, 125, 126, 129, 130, 131, 135, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 15 amino acid sequence DSYGEVGVRQAPFPS (PEP NO: and/or SEQ ID NO: 135). Such peptides form a group of peptides ("Group 83").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 53, 54, 55, 56, 57,
15 66, 67, 68, 69, 70, 80, 82, 83, 92, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 14 amino acid sequence DSYGEVGVRQAPFP (PEP NO: and/or SEQ ID NO: 138). Such peptides form a group of peptides ("Group 84").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 52, 53, 54, 55, 56,
20 57, 65, 66, 67, 68, 69, 70, 80, 82, 83, 92, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 13 amino acid sequence DSYGEVGVRQAPF (PEP NO: and/or SEQ ID NO: 137). Such peptides form a group of peptides ("Group 85").

25 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 51, 52, 53, 54, 55, 56, 57, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 92, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 149, 156, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 12 amino acid sequence
30 DSYGEVGVRQAP (PEP NO: and/or SEQ ID NO: 141). Such peptides form a group of peptides ("Group 86").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 50, 51, 52, 53, 54,

55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 92, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 148, 149, 155, 156, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 11 amino acid sequence DSYGEVGVRQA (PEP NO: and/or SEQ ID NO: 774). Such peptides
5 form a group of peptides ("Group 87").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 50, 51, 52, 53, 54, 55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 92, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137,
10 138, 141, 144, 146, 148, 149, 154, 155, 156, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 10 amino acid sequence DSYGEVGVRQ (PEP NO: and/or SEQ ID NO: 775). Such peptides form a group of peptides ("Group 88").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 50, 51, 52, 53, 54,
15 55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 92, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 146, 148, 149, 153, 154, 155, 156, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 9 amino acid sequence DSYGEVGVR (PEP NO: and/or SEQ ID NO: 776). Such peptides form a group of peptides ("Group 89").

20 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 50, 51, 52, 53, 54, 55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 92, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 146, 147, 148, 149, 153, 154, 155, 156, 159, 161, 291,
25 292, 293, 294, 295, 296, 297. Such peptides contain the 8 amino acid sequence DSYGEVGV (PEP NO: and/or SEQ ID NO: 777). Such peptides form a group of peptides ("Group 90").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 49, 50, 51, 52, 53, 54, 55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 92, 105, 106, 107, 108, 109, 110,
30 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 159, 161, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 7 amino acid sequence DSYGEVG (PEP NO: and/or SEQ ID NO: 778). Such peptides form a group of peptides ("Group 91").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 49, 50, 51, 52, 53, 54, 55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 92, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 159, 161, 192, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 6 amino acid sequence DSYGEV (PEP NO: and/or SEQ ID NO: 779). Such peptides form a group of peptides ("Group 92").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 49, 50, 51, 52, 53, 54, 55, 56, 57, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 92, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 143, 144, 146, 147, 148, 149, 151, 152, 153, 154, 155, 156, 159, 161, 192, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 5 amino acid sequence DSYGE (PEP NO: and/or SEQ ID NO: 780). Such peptides form a group of peptides ("Group 93").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 62, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 92, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 159, 161, 192, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 4 amino acid sequence DSYG (PEP NO: and/or SEQ ID NO: 781). Such peptides form a group of peptides ("Group 94").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 14, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 85, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 159, 161, 192, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence DSY (PEP NO: 782). Such peptides form a group of peptides ("Group 95").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 45, 57, 58, 70, 92, 158, 159, 160, 161. Such peptides contain the 17 amino acid sequence SYGEVGVRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 783). Such peptides form a group of peptides (“Group 96”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 29, 45, 56, 57, 58, 69, 70, 82, 92, 126, 158, 159, 160, 161, 162, 180, 186. Such peptides contain the 16 amino acid sequence SYGEVGVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 784). Such peptides form a group of peptides (“Group 97”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 45, 55, 56, 57, 58, 68, 69, 70, 82, 92, 125, 126, 131, 158, 159, 160, 161, 162, 180, 186. Such peptides contain the 15 amino acid sequence SYGEVGVRQAPFPSR (PEP NO: and/or SEQ ID NO: 785). Such peptides form a group of peptides (“Group 98”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 45, 54, 55, 56, 57, 58, 67, 68, 69, 70, 82, 86, 92, 124, 125, 126, 129, 130, 131, 135, 158, 159, 160, 161, 162, 180, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 14 amino acid sequence SYGEVGVRQAPFPS (PEP NO: and/or SEQ ID NO: 786). Such peptides form a group of peptides (“Group 99”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 45, 53, 54, 55, 56, 57, 58, 66, 67, 68, 69, 70, 80, 82, 83, 86, 92, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 158, 159, 160, 161, 162, 180, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 13 amino acid sequence SYGEVGVRQAPFP (PEP NO: and/or SEQ ID NO: 787). Such peptides form a group of peptides (“Group 100”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 45, 52, 53, 54, 55, 56, 57, 58, 65, 66, 67, 68, 69, 70, 80, 82, 83, 86, 92, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain

the 12 amino acid sequence SYGEVGVRQAPF (PEP NO: and/or SEQ ID NO: 788). Such peptides form a group of peptides ("Group 101").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 45, 51, 52, 53, 54, 55, 56, 57, 58, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 149, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 214, 221, 222, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 11 amino acid sequence SYGEVGVRQAP (PEP NO: and/or SEQ ID NO: 789). Such peptides form a group of peptides ("Group 102").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 45, 50, 51, 52, 53, 54, 55, 56, 57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 148, 149, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 213, 214, 221, 222, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 10 amino acid sequence SYGEVGVRQA (PEP NO: and/or SEQ ID NO: 790). Such peptides form a group of peptides ("Group 103").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 45, 50, 51, 52, 53, 54, 55, 56, 57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 146, 148, 149, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 212, 213, 214, 220, 221, 222, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 9 amino acid sequence SYGEVGVRQ (PEP NO: and/or SEQ ID NO: 791). Such peptides form a group of peptides ("Group 104").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 31, 32, 33, 34, 38, 39, 40, 41, 45, 50, 51, 52, 53, 54, 55, 56, 57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 146, 148, 149, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 212, 213, 214, 220, 221, 222, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides

contain the 8 amino acid sequence SYGEVGVR (PEP NO: and/or SEQ ID NO: 792). Such peptides form a group of peptides ("Group 105").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 45, 50, 51, 52, 53, 54, 55, 56, 57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 144, 146, 147, 148, 149, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 211, 212, 213, 214, 220, 221, 222, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 7 amino acid sequence SYGEVGV (PEP NO: and/or SEQ ID NO: 793). Such peptides form a group of peptides ("Group 106").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 45, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 211, 212, 213, 214, 219, 220, 221, 222, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 6 amino acid sequence SYGEVG (PEP NO: and/or SEQ ID NO: 794). Such peptides form a group of peptides ("Group 107").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 45, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 192, 211, 212, 213, 214, 217, 218, 219, 220, 221, 222, 226, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 5 amino acid sequence SYGEV (PEP NO: and/or SEQ ID NO: 795). Such peptides form a group of peptides ("Group 108").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 45, 49, 50, 51, 52, 53, 54, 55, 56,

57, 58, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 143, 144, 146, 147, 148, 149, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 192, 210, 211, 212, 213, 214, 217, 218, 219, 220, 221, 222, 225, 226, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 4 amino acid sequence SYGE (PEP NO: and/or SEQ ID NO: 796). Such peptides form a group of peptides ("Group 109").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 45, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 62, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 192, 209, 210, 211, 212, 213, 214, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 3 amino acid sequence SYG (PEP NO: 797). Such peptides form a group of peptides ("Group 110").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 43, 45, 46, 57, 58, 59, 70, 92, 139, 158, 159, 160, 161. Such peptides contain the 16 amino acid sequence YGEVGVRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 798). Such peptides form a group of peptides ("Group 111").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 29, 43, 45, 46, 56, 57, 58, 59, 69, 70, 82, 92, 126, 139, 158, 159, 160, 161, 162, 180, 186. Such peptides contain the 15 amino acid sequence YGEVGVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 799). Such peptides form a group of peptides ("Group 112").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 45, 46, 55, 56, 57, 58, 59, 68, 69, 70, 82, 92, 125, 126, 131, 139, 158, 159, 160, 161, 162, 180, 186. Such peptides contain the 14 amino acid sequence YGEVGVRQAPFPSR (PEP NO: and/or SEQ ID NO: 800). Such peptides form a group of peptides ("Group 113").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 45, 46, 54, 55, 56, 57, 58, 59, 67, 68, 69, 70, 82, 86, 92, 124, 125, 126, 129, 130, 131, 135, 139, 158, 159, 160, 161, 162, 180, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 13 amino acid sequence YGEVGVRQAPFPS (PEP NO: and/or SEQ ID NO: 801). Such peptides form a group of peptides ("Group 114").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 45, 46, 53, 54, 55, 56, 57, 58, 59, 66, 67, 68, 69, 70, 80, 82, 83, 86, 92, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 158, 159, 160, 161, 162, 180, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 12 amino acid sequence YGEVGVRQAPFP (PEP NO: and/or SEQ ID NO: 802). Such peptides form a group of peptides ("Group 115").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 43, 45, 46, 52, 53, 54, 55, 56, 57, 58, 59, 65, 66, 67, 68, 69, 70, 80, 82, 83, 86, 92, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 11 amino acid sequence YGEVGVRQAPF (PEP NO: and/or SEQ ID NO: 803). Such peptides form a group of peptides ("Group 116").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 43, 45, 46, 51, 52, 53, 54, 55, 56, 57, 58, 59, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 149, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 214, 221, 222, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 10 amino acid sequence YGEVGVRQAP (PEP NO: and/or SEQ ID NO: 804). Such peptides form a group of peptides ("Group 117").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 43, 45, 46, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 148, 149, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 213, 214, 221, 222, 230, 231,

291, 292, 293, 294, 295, 296, 297. Such peptides contain the 9 amino acid sequence YGEVGVRQA (PEP NO: and/or SEQ ID NO: 805). Such peptides form a group of peptides (“Group 118”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 32, 33, 34, 38, 39, 40, 41, 43, 45, 46, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 148, 149, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 212, 213, 214, 220, 221, 222, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 8 amino acid sequence YGEVGVRQ (PEP NO: and/or SEQ ID NO: 806). Such peptides form a group of peptides (“Group 119”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 31, 32, 33, 34, 38, 39, 40, 41, 43, 45, 46, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 86, 92, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 148, 149, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 212, 213, 214, 220, 221, 222, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 7 amino acid sequence YGEVGVR (PEP NO: and/or SEQ ID NO: 807). Such peptides form a group of peptides (“Group 120”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 43, 45, 46, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 144, 146, 147, 148, 149, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 211, 212, 213, 214, 220, 221, 222, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 6 amino acid sequence YGEVGV (PEP NO: and/or SEQ ID NO: 808). Such peptides form a group of peptides (“Group 121”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 43, 45, 46, 49, 50, 51, 52, 53, 54,

55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 211, 212, 213, 214, 219, 220, 221, 222, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 5 amino acid sequence YGEVG (PEP NO: and/or SEQ ID NO: 809). Such peptides form a group of peptides ("Group 122").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 43, 45, 46, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 143, 144, 146, 147, 148, 149, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 192, 211, 212, 213, 214, 217, 218, 219, 220, 221, 222, 226, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 4 amino acid sequence YGEV (PEP NO: and/or SEQ ID NO: 810). Such peptides form a group of peptides ("Group 123").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 10, 11, 12, 13, 14, 15, 16, 18, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 43, 45, 46, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 63, 64, 65, 66, 67, 68, 69, 70, 79, 80, 82, 83, 84, 86, 92, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 143, 144, 146, 147, 148, 149, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 165, 180, 186, 187, 188, 192, 210, 211, 212, 213, 214, 217, 218, 219, 220, 221, 222, 225, 226, 227, 228, 229, 230, 231, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 3 amino acid sequence YGE (PEP NO: 811). Such peptides form a group of peptides ("Group 124").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 43, 44, 45, 46, 47, 57, 58, 59, 60, 70, 85, 88, 89, 90, 91, 92, 139, 158, 159, 160, 161. Such peptides contain the 15 amino acid sequence GEVGVQRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 812). Such peptides form a group of peptides ("Group 125").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19,

29, 43, 44, 45, 46, 47, 56, 57, 58, 59, 60, 69, 70, 82, 85, 88, 89, 90, 91, 92, 126, 139, 158, 159, 160, 161, 162, 164, 180, 186. Such peptides contain the 14 amino acid sequence

GEVGVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 813). Such peptides form a group of peptides ("Group 126").

- 5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 44, 45, 46, 47, 55, 56, 57, 58, 59, 60, 68, 69, 70, 82, 85, 88, 89, 90, 91, 92, 125, 126, 131, 139, 158, 159, 160, 161, 162, 164, 180, 186. Such peptides contain the 13 amino acid sequence GEVGVRQAPFPSR (PEP NO: and/or SEQ ID NO: 814). Such peptides form a group of peptides ("Group 127").
- 10

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 44, 45, 46, 47, 54, 55, 56, 57, 58, 59, 60, 67, 68, 69, 70, 76, 82, 85, 86, 88, 89, 90, 91, 92, 124, 125, 126, 129, 130, 131, 135, 139, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 12 amino acid sequence GEVGVRQAPFPS (PEP NO: and/or SEQ ID NO: 815). Such peptides form a group of peptides ("Group 128").

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- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 44, 45, 46, 47, 53, 54, 55, 56, 57, 58, 59, 60, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 88, 89, 90, 91, 92, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 11 amino acid sequence GEVGVRQAPFP (PEP NO: and/or SEQ ID NO: 816). Such peptides form a group of peptides ("Group 129").
- 20
- 25

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 52, 53, 54, 55, 56, 57, 58, 59, 60, 65, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 183, 184, 185, 186, 187, 188, 189, 291, 292, 293, 294, 295, 296, 297. Such peptides contain the 10 amino acid sequence GEVGVRQAPF (PEP NO: and/or SEQ ID NO: 817). Such peptides form a group of peptides ("Group 130").
- 30

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 43, 44, 45, 46, 47, 57, 58, 59, 60, 61, 70, 85, 88, 89, 90, 91, 92, 93, 94, 95, 139, 158, 159, 160, 161, 208. Such peptides contain the 14 amino acid sequence EVGVRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 818). Such peptides form a group of peptides (“Group 131”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 43, 44, 45, 46, 47, 56, 57, 58, 59, 60, 61, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 126, 139, 158, 159, 160, 161, 162, 164, 180, 186, 208. Such peptides contain the 13 amino acid sequence EVGVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 819). Such peptides form a group of peptides (“Group 132”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 44, 45, 46, 47, 55, 56, 57, 58, 59, 60, 61, 68, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 125, 126, 131, 139, 158, 159, 160, 161, 162, 164, 180, 186, 208. Such peptides contain the 12 amino acid sequence EVGVRQAPFPSR (PEP NO: and/or SEQ ID NO: 820). Such peptides form a group of peptides (“Group 133”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 44, 45, 46, 47, 54, 55, 56, 57, 58, 59, 60, 61, 67, 68, 69, 70, 76, 82, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 124, 125, 126, 129, 130, 131, 135, 139, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 208, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 11 amino acid sequence EVGVRQAPFPS (PEP NO: and/or SEQ ID NO: 821). Such peptides form a group of peptides (“Group 134”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 44, 45, 46, 47, 53, 54, 55, 56, 57, 58, 59, 60, 61, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 208, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 10 amino acid sequence EVGVRQAPFP (PEP NO: and/or SEQ ID NO: 822). Such peptides form a group of peptides (“Group 135”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 65, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 183, 184, 185, 186, 187, 188, 189, 208, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 9 amino acid sequence EVGVRQAPF (PEP NO: and/or SEQ ID NO: 823). Such peptides form a group of peptides ("Group 136").

10 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 43, 44, 45, 46, 47, 48, 57, 58, 59, 60, 61, 62, 70, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 139, 142, 145, 150, 158, 159, 160, 161, 208, 209, 215. Such peptides contain the 13 amino acid sequence VGVRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 824). Such peptides form a group of peptides ("Group 137").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 43, 44, 45, 46, 47, 48, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 126, 139, 142, 145, 150, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 215. Such peptides contain the 12 amino acid sequence VGVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 825). Such peptides form a group of peptides ("Group 138").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 44, 45, 46, 47, 48, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 125, 126, 131, 139, 142, 145, 150, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 215. Such peptides contain the 11 amino acid sequence VGVRQAPFPSR (PEP NO: and/or SEQ ID NO: 826). Such peptides form a group of peptides ("Group 139").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 44, 45, 46, 47, 48, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67, 68, 69, 70, 76, 82, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 124, 125, 126, 129, 130, 131, 135, 139, 142, 145, 150, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 208, 209, 215, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 10

amino acid sequence VGVRQAPFPS (PEP NO: and/or SEQ ID NO: 827). Such peptides form a group of peptides ("Group 140").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 44, 45, 46, 47, 48, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 142, 145, 150, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 208, 209, 215, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 9 amino acid sequence VGVRQAPFP (PEP NO: and/or SEQ ID NO: 828). Such peptides form a group of peptides ("Group 141").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 142, 145, 150, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 183, 184, 185, 186, 187, 188, 189, 208, 209, 215, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 8 amino acid sequence VGVRQAPF (PEP NO: and/or SEQ ID NO: 829). Such peptides form a group of peptides ("Group 142").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 43, 44, 45, 46, 47, 48, 57, 58, 59, 60, 61, 62, 70, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 139, 142, 145, 150, 151, 158, 159, 160, 161, 208, 209, 210, 215, 216, 223, 224. Such peptides contain the 12 amino acid sequence GVRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 830). Such peptides form a group of peptides ("Group 143").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 43, 44, 45, 46, 47, 48, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 126, 139, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 215, 216, 223, 224. Such peptides contain the 11 amino acid sequence GVRQAPFPSRA (PEP NO: and/or SEQ ID NO: 831). Such peptides form a group of peptides ("Group 144").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 44, 45, 46, 47, 48, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 125, 126, 131, 139, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 215, 216, 223, 224. Such peptides contain the 10 amino acid sequence GVRQAPFPSR (PEP NO: and/or SEQ ID NO: 832). Such peptides form a group of peptides ("Group 145").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 44, 45, 46, 47, 48, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67, 68, 69, 70, 76, 82, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 124, 125, 126, 129, 130, 131, 135, 139, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 208, 209, 210, 215, 216, 223, 224, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 9 amino acid sequence GVRQAPFPS (PEP NO: and/or SEQ ID NO: 833). Such peptides form a group of peptides ("Group 146").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 44, 45, 46, 47, 48, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 166, 180, 181, 185, 186, 187, 188, 208, 209, 210, 215, 216, 223, 224, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 8 amino acid sequence GVRQAPFP (PEP NO: and/or SEQ ID NO: 834). Such peptides form a group of peptides ("Group 147").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 142, 145, 150, 151, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 208, 209, 210, 215, 216, 223, 224, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 7 amino acid sequence GVRQAPF (PEP NO: and/or SEQ ID NO: 835). Such peptides form a group of peptides ("Group 148").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 43, 44, 45, 46, 47, 48, 57, 58, 59, 60, 61, 62, 70, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 139, 142, 145, 150, 151, 158, 159, 160, 161, 208, 209, 210, 215, 216, 217, 218, 223, 224. Such peptides contain the 11 amino acid sequence VRQAPFPSRAS (PEP NO: and/or SEQ ID NO: 836). Such peptides form a group of peptides ("Group 149").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 43, 44, 45, 46, 47, 48, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 126, 139, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 215, 216, 217, 218, 223, 224. Such peptides contain the 10 amino acid sequence VRQAPFPSRA (PEP NO: and/or SEQ ID NO: 837). Such peptides form a group of peptides ("Group 150").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 44, 45, 46, 47, 48, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 125, 126, 131, 139, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 215, 216, 217, 218, 223, 224. Such peptides contain the 9 amino acid sequence VRQAPFPSR (PEP NO: and/or SEQ ID NO: 838). Such peptides form a group of peptides ("Group 151").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 44, 45, 46, 47, 48, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67, 68, 69, 70, 76, 82, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 124, 125, 126, 129, 130, 131, 135, 139, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 192, 208, 209, 210, 215, 216, 217, 218, 223, 224, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 8 amino acid sequence VRQAPFPS (PEP NO: and/or SEQ ID NO: 839). Such peptides form a group of peptides ("Group 152").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 44, 45, 46, 47, 48, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139,

140, 142, 145, 150, 151, 158, 159, 160, 161, 162, 164, 166, 180, 181, 185, 186, 187, 188, 192, 208, 209, 210, 215, 216, 217, 218, 223, 224, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 7 amino acid sequence VRQAPFP (PEP NO: and/or SEQ ID NO: 840). Such peptides form a group of peptides (“Group 153”).

5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 76, 77, 78, 80, 81, 82, 83, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 122, 123, 10 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 142, 145, 150, 151, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 192, 208, 209, 210, 215, 216, 217, 218, 223, 224, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 6 amino acid sequence VRQAPF (PEP NO: and/or SEQ ID NO: 841). Such peptides form a group of peptides (“Group 154”).

15 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 43, 44, 45, 46, 47, 48, 49, 57, 58, 59, 60, 61, 62, 70, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 139, 142, 143, 145, 150, 151, 152, 158, 159, 160, 161, 208, 209, 210, 215, 216, 217, 218, 223, 224, 225. Such peptides contain the 10 amino acid 20 sequence RQAPFPSRAS (PEP NO: and/or SEQ ID NO: 842). Such peptides form a group of peptides (“Group 155”).

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 43, 44, 45, 46, 47, 48, 49, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 25 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 126, 139, 142, 143, 145, 150, 151, 152, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 215, 216, 217, 218, 223, 224, 225. Such peptides contain the 9 amino acid sequence RQAPFPSRA (PEP NO: and/or SEQ ID NO: 843). Such peptides form a group of peptides (“Group 156”).

In some embodiments, the present invention provides a peptide comprising the amino acid 30 sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 43, 44, 45, 46, 47, 48, 49, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 125, 126, 131, 139, 142, 143, 145, 150, 151, 152, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 215, 216,

217, 218, 223, 224, 225. Such peptides contain the 8 amino acid sequence RQAPFPSR (PEP NO: and/or SEQ ID NO: 844). Such peptides form a group of peptides ("Group 157").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67, 68, 69, 70, 76, 82, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 124, 125, 126, 129, 130, 131, 135, 139, 142, 143, 145, 150, 151, 152, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 192, 208, 209, 210, 215, 216, 217, 218, 223, 224, 225, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 7 amino acid sequence RQAPFPS (PEP NO: and/or SEQ ID NO: 845). Such peptides form a group of peptides ("Group 158").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 80, 81, 82, 83, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 142, 143, 145, 150, 151, 152, 158, 159, 160, 161, 162, 164, 166, 180, 181, 185, 186, 187, 188, 192, 208, 209, 210, 215, 216, 217, 218, 223, 224, 225, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 6 amino acid sequence RQAPFP (PEP NO: and/or SEQ ID NO: 846). Such peptides form a group of peptides ("Group 159").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 33, 34, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 142, 143, 145, 150, 151, 152, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 192, 208, 209, 210, 215, 216, 217, 218, 223, 224, 225, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 5 amino acid sequence RQAPF (PEP NO: and/or SEQ ID NO: 847). Such peptides form a group of peptides ("Group 160").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19,

30, 43, 44, 45, 46, 47, 48, 49, 57, 58, 59, 60, 61, 62, 70, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 139, 142, 143, 145, 147, 150, 151, 152, 158, 159, 160, 161, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226. Such peptides contain the 9 amino acid sequence QAPFPSRAS (PEP NO: and/or SEQ ID NO: 848).

5 Such peptides form a group of peptides ("Group 161").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 30, 43, 44, 45, 46, 47, 48, 49, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 126, 139, 142, 143, 145, 10 147, 150, 151, 152, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226. Such peptides contain the 8 amino acid sequence QAPFPSRA (PEP NO: and/or SEQ ID NO: 849). Such peptides form a group of peptides ("Group 162").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 15 28, 29, 30, 43, 44, 45, 46, 47, 48, 49, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 125, 126, 131, 139, 142, 143, 145, 147, 150, 151, 152, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226. Such peptides contain the 7 amino acid sequence QAPFPSR (PEP NO: and/or SEQ ID NO: 850). Such peptides form a group of peptides ("Group 163").

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In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 30, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67, 68, 69, 70, 76, 82, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 25 105, 106, 107, 108, 124, 125, 126, 129, 130, 131, 135, 139, 142, 143, 145, 147, 150, 151, 152, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 192, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 6 amino acid sequence QAPFPS (PEP NO: and/or SEQ ID NO: 851). Such peptides form a group of peptides ("Group 164").

30 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 80, 81, 82, 83, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 123,

124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 142, 143, 145, 147, 150, 151, 152, 158, 159, 160, 161, 162, 164, 166, 180, 181, 185, 186, 187, 188, 192, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 5 amino acid sequence QAPFP (PEP NO: and/or SEQ ID
5 NO: 852). Such peptides form a group of peptides ("Group 165").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 74,
10 75, 76, 77, 78, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 142, 143, 145, 147, 150, 151, 152, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 192, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301,
15 302, 303, 304. Such peptides contain the 4 amino acid sequence QAPF (PEP NO: and/or SEQ ID NO: 853). Such peptides form a group of peptides ("Group 166").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42,
20 43, 44, 45, 46, 47, 48, 49, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 138, 139, 140, 141, 142, 143, 144, 145, 147, 149, 150, 151, 152, 156, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168,
25 180, 181, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 203, 205, 208, 209, 210, 211, 214, 215, 216, 217, 218, 219, 221, 222, 223, 224, 225, 226, 231, 234, 235, 252, 272, 273, 277, 278, 279, 280, 281, 282, 283, 284, 285, 286, 287, 288, 289, 290, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence QAP (PEP NO: 854). Such peptides form a group of peptides
30 ("Group 167").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 30, 31, 43, 44, 45, 46, 47, 48, 49, 57, 58, 59, 60, 61, 62, 70, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 139, 142, 143, 145,

147, 150, 151, 152, 153, 158, 159, 160, 161, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227. Such peptides contain the 8 amino acid sequence APFPSRAS (PEP NO: and/or SEQ ID NO: 855). Such peptides form a group of peptides (“Group 168”).

In some embodiments, the present invention provides a peptide comprising the amino acid
5 sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 30, 31, 43, 44, 45, 46, 47, 48, 49, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 126, 139, 142, 143, 145, 147, 150, 151, 152, 153, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227. Such peptides contain the 7 amino
10 acid sequence APFPSRA (PEP NO: and/or SEQ ID NO: 856). Such peptides form a group of peptides (“Group 169”).

In some embodiments, the present invention provides a peptide comprising the amino acid
sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19,
28, 29, 30, 31, 43, 44, 45, 46, 47, 48, 49, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 84, 85, 88,
15 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 125, 126, 131, 139, 142, 143, 145, 147, 150, 151, 152, 153, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227. Such peptides
contain the 6 amino acid sequence APFPSR (PEP NO: and/or SEQ ID NO: 857). Such peptides
form a group of peptides (“Group 170”).

20 In some embodiments, the present invention provides a peptide comprising the amino acid
sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19,
25, 26, 28, 29, 30, 31, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67,
68, 69, 70, 76, 82, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103,
104, 105, 106, 107, 108, 109, 110, 111, 124, 125, 126, 129, 130, 131, 135, 139, 142, 143, 145,
25 147, 150, 151, 152, 153, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 192, 208,
209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 291, 292, 293, 294, 295, 296,
297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 5 amino acid sequence APFPS
(PEP NO: and/or SEQ ID NO: 858). Such peptides form a group of peptides (“Group 171”).

In some embodiments, the present invention provides a peptide comprising the amino acid
30 sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15,
16, 19, 25, 26, 27, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 53, 54,
55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 80, 81, 82, 83, 84, 85,
86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108,
109, 110, 111, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 142, 143, 145, 147,

150, 151, 152, 153, 158, 159, 160, 161, 162, 164, 166, 180, 181, 185, 186, 187, 188, 192, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 4 amino acid sequence APFP (PEP NO: and/or SEQ ID NO: 859). Such peptides form a group of peptides ("Group 172").

- 5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 65, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 122, 123, 124, 125, 126, 128, 129, 130, 131, 133, 134, 135, 137, 138, 139, 140, 142, 143, 145, 147, 150, 151, 152, 153, 157, 158, 159, 160, 161, 162, 163, 164, 165, 166, 168, 180, 181, 183, 184, 185, 186, 187, 188, 189, 192, 208, 209, 210, 211, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence
- 15 APF (PEP NO: 860). Such peptides form a group of peptides ("Group 173").

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 57, 58, 59, 60, 61, 62, 70, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114,
- 20 139, 142, 143, 145, 146, 147, 150, 151, 152, 153, 154, 158, 159, 160, 161, 208, 209, 210, 211, 212, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 228. Such peptides contain the 7 amino acid sequence PFPSRAS (PEP NO: and/or SEQ ID NO: 861). Such peptides form a group of peptides ("Group 174").

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19,
- 25 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 56, 57, 58, 59, 60, 61, 62, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 126, 139, 142, 143, 145, 146, 147, 150, 151, 152, 153, 154, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227,
- 30 228. Such peptides contain the 6 amino acid sequence PFPSRA (PEP NO: and/or SEQ ID NO: 862). Such peptides form a group of peptides ("Group 175").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 55, 56, 57, 58, 59, 60, 61, 62, 68, 69, 70, 82, 84, 85,

88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 125, 126, 131, 139, 142, 143, 145, 146, 147, 150, 151, 152, 153, 154, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 228. Such peptides contain the 5 amino acid sequence PFPSR (PEP NO: 5 and/or SEQ ID NO: 863). Such peptides form a group of peptides ("Group 176").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 30, 31, 32, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 54, 55, 56, 57, 58, 59, 60, 61, 62, 67, 68, 69, 70, 76, 82, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 124, 125, 126, 129, 130, 131, 135, 139, 142, 143, 145, 146, 147, 150, 151, 152, 153, 154, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 192, 208, 209, 210, 211, 212, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 228, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 4 amino acid sequence PFPS (PEP NO: and/or SEQ ID NO: 864). Such peptides 15 form a group of peptides ("Group 177").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 1, 2, 3, 4, 5, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 66, 67, 68, 69, 70, 71, 72, 74, 75, 76, 77, 78, 80, 81, 82, 83, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 123, 124, 125, 126, 129, 130, 131, 134, 135, 138, 139, 140, 142, 143, 145, 146, 147, 150, 151, 152, 153, 154, 158, 159, 160, 161, 162, 164, 166, 180, 181, 185, 186, 187, 188, 192, 208, 209, 210, 211, 212, 215, 216, 217, 218, 219, 223, 224, 225, 226, 227, 228, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304, 307, 308. Such 25 peptides contain the 3 amino acid sequence PFP (PEP NO: 865). Such peptides form a group of peptides ("Group 178").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 57, 58, 59, 60, 61, 62, 63, 70, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 139, 142, 143, 145, 146, 147, 148, 150, 151, 152, 153, 154, 155, 158, 159, 160, 161, 208, 209, 210, 211, 212, 213, 215, 216, 217, 218, 219, 220, 223, 224, 225, 226, 227, 228. Such peptides contain the 6 amino acid sequence FPSRAS (PEP NO: and/or SEQ ID NO: 866). Such peptides form a group of peptides ("Group 179").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 56, 57, 58, 59, 60, 61, 62, 63, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 126, 139, 142, 143, 145, 146, 147, 148, 150, 151, 152, 153, 154, 155, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 213, 215, 216, 217, 218, 219, 220, 223, 224, 225, 226, 227, 228. Such peptides contain the 5 amino acid sequence FPSRA (PEP NO: and/or SEQ ID NO: 867). Such peptides form a group of peptides ("Group 180").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 55, 56, 57, 58, 59, 60, 61, 62, 63, 68, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 125, 126, 131, 139, 142, 143, 145, 146, 147, 148, 150, 151, 152, 153, 154, 155, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 213, 215, 216, 217, 218, 219, 220, 223, 224, 225, 226, 227, 228. Such peptides contain the 4 amino acid sequence FPSR (PEP NO: and/or SEQ ID NO: 868). Such peptides form a group of peptides ("Group 181").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 9, 10, 11, 12, 13, 14, 15, 16, 19, 25, 26, 28, 29, 30, 31, 32, 38, 39, 40, 43, 44, 45, 46, 47, 48, 49, 50, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 67, 68, 69, 70, 76, 82, 84, 85, 86, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 124, 125, 126, 129, 130, 131, 135, 139, 142, 143, 145, 146, 147, 148, 150, 151, 152, 153, 154, 155, 158, 159, 160, 161, 162, 164, 166, 180, 185, 186, 187, 188, 192, 208, 209, 210, 211, 212, 213, 215, 216, 217, 218, 219, 220, 223, 224, 225, 226, 227, 228, 291, 292, 293, 294, 295, 296, 297, 298, 299, 300, 301, 302, 303, 304. Such peptides contain the 3 amino acid sequence FPS (PEP NO: 869). Such peptides form a group of peptides ("Group 182").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 19, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 51, 57, 58, 59, 60, 61, 62, 63, 64, 70, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 139, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229. Such peptides contain the

5 amino acid sequence PSRAS (PEP NO: and/or SEQ ID NO: 870). Such peptides form a group of peptides ("Group 183").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 19, 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 51, 56, 57, 58, 59, 60, 61, 62, 63, 64, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 126, 139, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229. Such peptides contain the 4 amino acid sequence PSRA (PEP NO: and/or SEQ ID NO: 871). Such peptides form a group of peptides ("Group 184").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 19, 28, 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 51, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 68, 69, 70, 82, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 125, 126, 131, 139, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229. Such peptides contain the 3 amino acid sequence PSR (PEP NO: 872). Such peptides form a group of peptides ("Group 185").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 57, 58, 59, 60, 61, 62, 63, 64, 65, 70, 83, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 139, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230. Such peptides contain the 4 amino acid sequence SRAS (PEP NO: and/or SEQ ID NO: 873). Such peptides form a group of peptides ("Group 186").

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 29, 30, 31, 32, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 69, 70, 82, 83, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 126, 139, 142,

143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 162, 164, 180, 186, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230. Such peptides contain the 3 amino acid sequence SRA (PEP NO: 874). Such peptides form a group of peptides ("Group 187").

- 5 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any one of PEP NOs: and/or SEQ ID NOs: 2, 3, 6, 7, 9, 10, 11, 12, 13, 14, 15, 16, 18, 19, 27, 30, 31, 32, 35, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 70, 83, 84, 85, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 127, 139, 10 140, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 158, 159, 160, 161, 208, 209, 210, 211, 212, 213, 214, 215, 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, 230, 231. Such peptides contain the 3 amino acid sequence RAS (PEP NO: 875). Such peptides form a group of peptides ("Group 188").

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 774-875 wherein the peptide has delta opioid agonist activity.
- 15

2.7. Consensus Sequences

- Peptides comprising PEP NOs: and/or SEQ ID NOs: 1-304, or various structural and/or functional subgroupings of those peptides, can also be described using consensus amino acid sequences based on an alignment as in **Fig. 1A-F**. For example, in some embodiments, the present invention provides a peptide comprising the amino acid sequence:
- 20

$X_2X_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}$ (PEP NO: 316),

wherein the numbers in subscript are the amino acid positions, numbered as in **Fig. 1A-F**, and wherein, independently of each other:

- 25 X_2 is D, K, or R;
 X_3 is G, K, S, or W;
 X_4 is A, D, F, G, K, W, or Y;
 X_5 is A, C, D, E, G, H, K, N, S, or Y;
 X_6 is A, D, E, G, I, K, L, Q, or V;
30 X_7 is A, E, G, I, L, M, V, or W;
 X_8 is A, D, G, S, or V;
 X_9 is A, C, F, H, I, K, L, P, Q, R, T, V, or W;
 X_{10} is A, C, D, E, G, H, K, P, Q, R, V, W, or Y;

X₁₁ is A, E, H, N, Q, or R;

X₁₂ is A, G, L, P, Q, T, or V;

X₁₃ is A, K, P, or S;

X₁₄ is A, F, I, K, L, or Y;

5 X₁₅ is K, L, P, or V;

X₁₆ is A, K, L, P, or S;

X₁₇ is A, C, D, H, K, N, Q, R, S, or Y;

X₁₈ is A, G, I, K, or V; and

X₁₉ is A, D, F, K, or S.

- 10 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 316 wherein the peptide has delta opioid agonist activity.

In some embodiments, the present invention provides peptides comprising the amino acid sequence:

- 15 D₂S₃Y₄G₅E₆V₇G₈V₉R₁₀Q₁₁A₁₂P₁₃F₁₄P₁₅S₁₆X₁₇A₁₈S₁₉ (PEP NO: and/or SEQ ID NO: 317)
wherein the numbers in subscript are the amino acid positions, numbered as in **Fig. 1A-F**,
and wherein X₁₇ is K, Q, R or S.

- In some embodiments, the present invention provides a peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 317 wherein the peptide has delta opioid agonist
20 activity.

In some embodiments, the present invention provides a peptide comprising the amino acid sequence:

- 25 X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 318),
X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 319),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 320),
X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 321),
X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 322),
X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 323),
X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 324),
30 X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 325),
X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 326),
X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 327),
X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 328),

- X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 329),
X₁₅X₁₆X₁₇X₁₈X₁₉ (PEP NO: 330),
X₁₆X₁₇X₁₈X₁₉ (PEP NO: 331),
X₁₇X₁₈X₁₉ (PEP NO: 332),
- 5 X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 333),
X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 334),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 335),
X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 336),
X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 337),
- 10 X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 338),
X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 339),
X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 340),
X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 341),
X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 342),
- 15 X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 343),
X₁₄X₁₅X₁₆X₁₇X₁₈ (PEP NO: 344),
X₁₅X₁₆X₁₇X₁₈ (PEP NO: 345),
X₁₆X₁₇X₁₈ (PEP NO: 346),
X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 347),
- 20 X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 348),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 349),
X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 350),
X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 351),
X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 352),
- 25 X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 353),
X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 354),
X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 355),
X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 356),
X₁₃X₁₄X₁₅X₁₆X₁₇ (PEP NO: 357),
- 30 X₁₄X₁₅X₁₆X₁₇ (PEP NO: 358),
X₁₅X₁₆X₁₇ (PEP NO: 359),
X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 360),
X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 361),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 362),
- 35 X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 363),

- X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 364),
X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 365),
X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 366),
X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 367),
5 X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 368),
X₁₂X₁₃X₁₄X₁₅X₁₆ (PEP NO: 369),
X₁₃X₁₄X₁₅X₁₆ (PEP NO: 370),
X₁₄X₁₅X₁₆ (PEP NO: 371),
X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 372),
10 X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 373),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 374),
X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 375),
X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 376),
X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 377),
15 X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 378),
X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 379),
X₁₁X₁₂X₁₃X₁₄X₁₅ (PEP NO: 380),
X₁₂X₁₃X₁₄X₁₅ (PEP NO: 381),
X₁₃X₁₄X₁₅ (PEP NO: 382),
20 X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 383),
X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 384),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 385),
X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 386),
X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 387),
25 X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 388),
X₉X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 389),
X₁₀X₁₁X₁₂X₁₃X₁₄ (PEP NO: 390),
X₁₁X₁₂X₁₃X₁₄ (PEP NO: 391),
X₁₂X₁₃X₁₄ (PEP NO: 392),
30 X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 393),
X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 394),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 395),
X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 396),
X₇X₈X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 397),
35 X₈X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 398),

- X₉X₁₀X₁₁X₁₂X₁₃ (PEP NO: 399),
X₁₀X₁₁X₁₂X₁₃ (PEP NO: 400),
X₁₁X₁₂X₁₃ (PEP NO: 401),
X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂ (PEP NO: 402),
5 X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂ (PEP NO: 403),
X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂ (PEP NO: 404),
X₆X₇X₈X₉X₁₀X₁₁X₁₂ (PEP NO: 405),
X₇X₈X₉X₁₀X₁₁X₁₂ (PEP NO: 406),
X₈X₉X₁₀X₁₁X₁₂ (PEP NO: 407),
10 X₉X₁₀X₁₁X₁₂ (PEP NO: 408),
X₁₀X₁₁X₁₂ (PEP NO: 409),
X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁ (PEP NO: 410),
X₄X₅X₆X₇X₈X₉X₁₀X₁₁ (PEP NO: 411),
X₅X₆X₇X₈X₉X₁₀X₁₁ (PEP NO: 412),
15 X₆X₇X₈X₉X₁₀X₁₁ (PEP NO: 413),
X₇X₈X₉X₁₀X₁₁ (PEP NO: 414),
X₈X₉X₁₀X₁₁ (PEP NO: 415),
X₉X₁₀X₁₁ (PEP NO: 416),
X₃X₄X₅X₆X₇X₈X₉X₁₀ (PEP NO: 417),
20 X₄X₅X₆X₇X₈X₉X₁₀ (PEP NO: 418),
X₅X₆X₇X₈X₉X₁₀ (PEP NO: 419),
X₆X₇X₈X₉X₁₀ (PEP NO: 420),
X₇X₈X₉X₁₀ (PEP NO: 421),
X₈X₉X₁₀ (PEP NO: 422),
25 X₃X₄X₅X₆X₇X₈X₉ (PEP NO: 423),
X₄X₅X₆X₇X₈X₉ (PEP NO: 424),
X₅X₆X₇X₈X₉ (PEP NO: 425),
X₆X₇X₈X₉ (PEP NO: 426),
X₇X₈X₉ (PEP NO: 427),
30 X₃X₄X₅X₆X₇X₈ (PEP NO: 428),
X₄X₅X₆X₇X₈ (PEP NO: 429),
X₅X₆X₇X₈ (PEP NO: 430),
X₆X₇X₈ (PEP NO: 431),
X₃X₄X₅X₆X₇ (PEP NO: 432),
35 X₄X₅X₆X₇ (PEP NO: 433),

X₅X₆X₇ (PEP NO: 434),

X₃X₄X₅X₆ (PEP NO: 435),

X₄X₅X₆ (PEP NO: 436), or

X₃X₄X₅ (PEP NO: 437),

- 5 Wherein, for each of these amino acid sequences, the numbers in subscript are the amino acid positions, numbered as in **Fig. 1A-F**, and wherein, independently of each other:

X₂ is D, K, or R;

X₃ is G, K, S, or W;

X₄ is A, D, F, G, K, W, or Y;

- 10 X₅ is A, C, D, E, G, H, K, N, S, or Y;

X₆ is A, D, E, G, I, K, L, Q, or V;

X₇ is A, E, G, I, L, M, V, or W;

X₈ is A, D, G, S, or V;

X₉ is A, C, F, H, I, K, L, P, Q, R, T, V, or W;

- 15 X₁₀ is A, C, D, E, G, H, K, P, Q, R, V, W, or Y;

X₁₁ is A, E, H, N, Q, or R;

X₁₂ is A, G, L, P, Q, T, or V;

X₁₃ is A, K, P, or S;

X₁₄ is A, F, I, K, L, or Y;

- 20 X₁₅ is K, L, P, or V;

X₁₆ is A, K, L, P, or S;

X₁₇ is A, C, D, H, K, N, Q, R, S, or Y;

X₁₈ is A, G, I, K, or V; and

X₁₉ is A, D, F, K, or S.

- 25 In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any of PEP NOs: 318-437. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any of PEP NOs: 318-437 wherein the peptide has delta opioid agonist activity.

- 30 In some embodiments, a peptide described in this section has delta opioid agonist activity. In some embodiments, a peptide described in this section has analgesic efficacy in a rodent model of pain as described in Example 5.

2.8. Retro-inverso Sequences

In some embodiments, the present invention provides a retro-inverso variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315 wherein the variant peptide has delta opioid agonist activity. In some embodiments, the present invention provides a retro-inverso variant of PEP NO: and/or SEQ ID NO: 316 or PEP NO: and/or SEQ ID NO: 317 wherein the variant peptide has delta opioid agonist activity. In some embodiments, the present invention provides a retro-inverso variant of any one of PEP NOs: and/or SEQ ID NOs: 318-437 wherein the variant peptide has delta opioid agonist activity. In some embodiments, the present invention provides a retro-inverso variant of any one of PEP NOs: and/or SEQ ID NOs: 753-875 wherein the variant peptide has delta opioid agonist activity. In some embodiments, the present invention provides a retro-inverso variant of any peptide of the present invention wherein the variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides a modified retro-inverso variant of any peptide of the present invention wherein the modified variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides an N-terminal palmitoylated retro-inverso variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides an N-terminal palmitoylated retro-inverso variant of PEP NO: and/or SEQ ID NO: 316 or PEP NO: and/or SEQ ID NO: 317. In some embodiments, the present invention provides an N-terminal palmitoylated retro-inverso variant of any one of PEP NOs: and/or SEQ ID NOs: 318-437. In some embodiments, the present invention provides an N-terminal palmitoylated retro-inverso variant of any one of PEP NOs: and/or SEQ ID NOs: 753-875.

PEP NOs: and/or SEQ ID NOs: 305-315 are examples of N-terminal palmitoylated retro-inverso peptides where the reference is the alignment of PEP NOs: and/or SEQ ID NOs: 1-304 as presented in **Fig. 1A-F**. For example, PEP NO: and/or SEQ ID NO: 311 is an N-terminal palmitoylated retro-inverso of PEP NO: and/or SEQ ID NO: 195.

The retro-inverso sequences of PEP NOs: and/or SEQ ID NOs: 1-315 are presented below in Table 4.

Table 4. Retro-inverso sequences of PEP NOs: and/or SEQ ID NOs: 1-315

PEP NO: and/or SEQ ID NO:	SEQ ID NO: of retro-inverso sequence	PEP NO: of retro-inverso sequence	Retro-inverso amino acid sequence
1	438	438	{dN}{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
2	439	439	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
3	440	440	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}

PEP NO: and/or SEQ ID NO:	SEQ ID NO: of retro-inverso sequence	PEP NO: of retro-inverso sequence	Retro-inverso amino acid sequence
4	441	441	{dN}{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}{dG}{dR}
5	442	442	{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}{dG}{dR}
6	443	443	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}{dG}{dR}
7	444	444	{dC}{dS}{dA}{dR}{dS}{dP}{dY}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}{dG}{dR}
8	445	445	{dC}{dF}{dA}{dR}{dS}{dL}{dY}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}{dG}{dR}
9	446	446	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}{dG}{dD}
10	447	447	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}{dG}{dR}
11	448	448	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
12	449	449	C{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
13	450	450	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
14	451	451	C{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
15	452	452	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
16	453	453	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
17	454	454	CSARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
18	455	455	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
19	456	456	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}{htt-cyclic-dD}
20	457	457	CSARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
21	458	458	CSARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
22	459	459	{r-peg40k-C}SARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
23	460	460	CSA{r-peg40k-dbcO}-{azide-dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
24	461	461	CSA{r-pal-dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
25	462	462	{dC}{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
26	463	463	{dN}{dC}{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
27	464	464	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
28	465	465	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
29	466	466	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
30	467	467	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
31	468	468	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
32	469	469	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
33	470	470	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
34	471	471	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
35	472	472	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
36	473	473	{dN}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
37	474	474	{dC}{dS}{dA}{dV}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
38	475	475	{dC}{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
39	476	476	{dC}{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
40	477	477	C{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
41	478	478	C{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
42	479	479	CSA{r-pal-dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
43	480	480	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
44	481	481	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
45	482	482	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
46	483	483	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
47	484	484	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
48	485	485	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
49	486	486	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
50	487	487	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
51	488	488	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
52	489	489	{dC}{dS}{dA}{dR}{dS}{dK}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
53	490	490	{dC}{dS}{dA}{dR}{dS}{dK}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
54	491	491	{dC}{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
55	492	492	{dC}{dS}{dK}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
56	493	493	{dC}{dK}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
57	494	494	{dK}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
58	495	495	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}

PEP NO: and/or SEQ ID NO:	SEQ ID NO: of retro-inverso sequence	PEP NO: of retro-inverso sequence	Retro-inverso amino acid sequence
59	496	496	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dD}
60	497	497	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dS}{dD}
61	498	498	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dY}{dS}{dD}
62	499	499	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dG}{dY}{dS}{dD}
63	500	500	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
64	501	501	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
65	502	502	{dC}{dS}{dA}{dR}{dS}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
66	503	503	{dC}{dS}{dA}{dR}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
67	504	504	{dC}{dS}{dA}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
68	505	505	{dC}{dS}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
69	506	506	{dC}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
70	507	507	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
71	508	508	{dN}{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dF}{dW}{dD}
72	509	509	{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
73	510	510	{dC}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
74	511	511	{dN}{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dG}{dW}{dI}{dG}{dW}
75	512	512	{dN}{dC}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dG}{dW}{dI}{dG}{dW}
76	513	513	{dC}{dS}{dI}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dC}
77	514	514	{dC}{dS}{dI}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
78	515	515	{dC}{dS}{dI}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
79	516	516	{dN}{dC}{dS}{dI}{dS}{dP}{dV}{dY}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
80	517	517	{dN}{dC}{dD}{dG}{dQ}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
81	518	518	{dC}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
82	519	519	{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}{dC}{dS}
83	520	520	{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}{dC}{dS}{dA}{dR}{dS}
84	521	521	{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}
85	522	522	{dY}{dS}{dD}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
86	523	523	{dC}{dS}{dA}{r-pal- {dK}}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
87	524	524	CSA{r-ste- {dK}}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{YS}{dD}
88	525	525	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dD}
89	526	526	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dA}
90	527	527	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dW}
91	528	528	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dG}
92	529	529	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
93	530	530	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dS}{dY}{dS}{dD}
94	531	531	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dD}{dY}{dS}{dD}
95	532	532	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dA}{dY}{dS}{dD}
96	533	533	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
97	534	534	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dD}{dG}{dY}{dS}{dD}
98	535	535	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dA}{dG}{dY}{dS}{dD}
99	536	536	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dI}{dE}{dG}{dY}{dS}{dD}
100	537	537	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dL}{dE}{dG}{dY}{dS}{dD}
101	538	538	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dM}{dE}{dG}{dY}{dS}{dD}
102	539	539	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dA}{dE}{dG}{dY}{dS}{dD}
103	540	540	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dS}{dV}{dE}{dG}{dY}{dS}{dD}
104	541	541	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dA}{dV}{dE}{dG}{dY}{dS}{dD}
105	542	542	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dI}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
106	543	543	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dL}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
107	544	544	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dA}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
108	545	545	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dH}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
109	546	546	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dH}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
110	547	547	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dE}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
111	548	548	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dA}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
112	549	549	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dG}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
113	550	550	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dT}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
114	551	551	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dL}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
115	552	552	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dS}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
116	553	553	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dA}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
117	554	554	{dC}{dS}{dA}{dR}{dS}{dP}{dY}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
118	555	555	{dC}{dS}{dA}{dR}{dS}{dP}{dL}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
119	556	556	{dC}{dS}{dA}{dR}{dS}{dP}{dI}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
120	557	557	{dC}{dS}{dA}{dR}{dS}{dP}{dY}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
121	558	558	{dC}{dS}{dA}{dR}{dS}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
122	559	559	{dC}{dS}{dA}{dR}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
123	560	560	{dC}{dS}{dA}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}

PEP NO: and/or SEQ ID NO:	SEQ ID NO: of retro-inverso sequence	PEP NO: of retro-inverso sequence	Retro-inverso amino acid sequence
124	561	561	{dC}{dS}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
125	562	562	{dC}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
126	563	563	{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
127	564	564	{dC}{dS}{dA}{dR}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
128	565	565	{dC}{dS}{dA}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
129	566	566	{dC}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
130	567	567	{dC}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
131	568	568	{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
132	569	569	{dC}{dS}{dA}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
133	570	570	{dC}{dS}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
134	571	571	{dC}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
135	572	572	{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
136	573	573	{dC}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
137	574	574	{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
138	575	575	{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
139	576	576	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dK}{dK}
140	577	577	{dC}{dS}{dA}{dR}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dD}
141	578	578	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
142	579	579	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
143	580	580	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
144	581	581	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
145	582	582	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
146	583	583	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
147	584	584	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
148	585	585	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
149	586	586	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
150	587	587	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
151	588	588	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
152	589	589	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
153	590	590	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
154	591	591	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
155	592	592	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
156	593	593	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
157	594	594	SA{r-pal-fdK}SP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}YS{BD}
158	595	595	{dR}{dR}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
159	596	596	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
160	597	597	{dR}{dR}{dR}{dR}{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
161	598	598	{dC}{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
162	599	599	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
163	600	600	{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
164	601	601	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
165	602	602	{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
166	603	603	{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
167	604	604	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
168	605	605	SARSP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}YS{BD}
169	606	606	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
170	607	607	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
171	608	608	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
172	609	609	{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
173	610	610	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
174	611	611	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
175	612	612	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
176	613	613	{dP}{dA}{dH}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
177	614	614	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
178	615	615	{dP}{dA}{dH}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
179	616	616	{dP}{dA}{dH}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
180	617	617	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
181	618	618	{dN}{dC}{dS}{dI}{dS}{dL}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
182	619	619	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
183	620	620	A{r-pal-fdK}SP{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}YS
184	621	621	{r-pal-fdK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}YS
185	622	622	{r-pal-fdK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
186	623	623	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
187	624	624	{dS}{dA}{r-pal-fdK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
188	625	625	{dS}{dA}{r-pal-fdK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}

PEP NO: and/or SEQ ID NO:	SEQ ID NO: of retro-inverso sequence	PEP NO: of retro-inverso sequence	Retro-inverso amino acid sequence
189	626	626	{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dE}{dG}{dY}
190	627	627	{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}
191	628	628	{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}
192	629	629	{dC}{dS}{dA}{r-pal- {dK}}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dD}{dV}{dE}{dG}{dY}{dS}{dD}
193	630	630	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
194	631	631	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}
195	632	632	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}
196	633	633	{dP}{dA}{dQ}{dR}{dV}{dG}
197	634	634	{dP}{dA}{dQ}{dR}{dV}
198	635	635	{dP}{dA}{dQ}{dR}
199		636	{dP}{dA}{dQ}
200	637	637	{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
201	638	638	{dQ}{dR}{dV}{dG}{dV}{dE}{dG}
202	639	639	{dR}{dV}{dG}{dV}{dE}{dG}
203	640	640	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}
204	641	641	{dR}{dV}{dG}{dV}
205	642	642	{dP}{dA}{dQ}{dR}{dV}{dG}
206	643	643	{dA}{dQ}{dR}{dV}{dG}
207		644	{dR}{dV}{dG}
208	645	645	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dY}{dS}{dD}
209	646	646	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dG}{dY}{dS}{dD}
210	647	647	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dE}{dG}{dY}{dS}{dD}
211	648	648	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
212	649	649	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
213	650	650	{dS}{dA}{dR}{dS}{dP}{dF}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
214	651	651	{dS}{dA}{dR}{dS}{dP}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
215	652	652	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dY}{dS}{dD}
216	653	653	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dG}{dY}{dS}{dD}
217	654	654	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dE}{dG}{dY}{dS}{dD}
218	655	655	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dE}{dG}{dY}{dS}{dD}
219	656	656	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
220	657	657	{dS}{dA}{dR}{dS}{dP}{dF}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
221	658	658	{dS}{dA}{dR}{dS}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
222	659	659	{dS}{dA}{dR}{dS}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
223	660	660	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dY}{dS}{dD}
224	661	661	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dY}{dS}{dD}
225	662	662	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dE}{dG}{dY}{dS}{dD}
226	663	663	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dQ}{dV}{dE}{dG}{dY}{dS}{dD}
227	664	664	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dA}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
228	665	665	{dS}{dA}{dR}{dS}{dP}{dF}{dP}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
229	666	666	{dS}{dA}{dR}{dS}{dP}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
230	667	667	{dS}{dA}{dR}{dS}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
231	668	668	{dS}{dA}{dR}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
232	669	669	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}
233	670	670	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dD}
234	671	671	{dR}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}
235	672	672	{dR}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dD}
236	673	673	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}
237	674	674	{dP}{dA}{dQ}{dR}{dV}{dG}{dE}
238	675	675	{dP}{dA}{dQ}{dR}{dV}{dV}{dE}
239	676	676	{dP}{dA}{dQ}{dV}{dG}{dV}{dE}
240	677	677	{dP}{dA}{dR}{dV}{dG}{dV}{dE}
241	678	678	{dP}{dQ}{dR}{dV}{dG}{dV}{dE}
242	679	679	{dA}{dQ}{dR}{dV}{dG}{dV}{dE}
243	680	680	{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dA}
244	681	681	{dP}{dA}{dQ}{dR}{dV}{dG}{dA}{dE}
245	682	682	{dP}{dA}{dQ}{dR}{dV}{dA}{dV}{dE}
246	683	683	{dP}{dA}{dQ}{dR}{dA}{dG}{dV}{dE}
247	684	684	{dP}{dA}{dQ}{dA}{dV}{dG}{dV}{dE}
248	685	685	{dP}{dA}{dA}{dR}{dV}{dG}{dV}{dE}
249	686	686	{dP}{dG}{dQ}{dR}{dV}{dG}{dV}{dE}
250	687	687	{dA}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}
251	688	688	{dR}{dV}{dG}{dV}{dE}{dG}
252	689	689	{dP}{dA}{dQ}{dR}{dV}
253	690	690	{dR}{dV}{dG}{dV}{dE}{dG}
254	691	691	{dR}{dV}{dG}{dV}{dG}{dE}
255	692	692	{dR}{dV}{dG}{dE}{dV}{dG}
256	693	693	{dR}{dV}{dV}{dG}{dE}{dG}

PEP NO: and/or SEQ ID NO:	SEQ ID NO: of retro-inverso sequence	PEP NO: of retro-inverso sequence	Retro-inverso amino acid sequence
257	694	694	{dK}{dV}{dG}{dV}{dE}{dG}
258	695	695	{dD}{dV}{dG}{dV}{dE}{dG}
259	696	696	{dE}{dV}{dG}{dV}{dE}{dG}
260	697	697	{dW}{dV}{dG}{dV}{dE}{dG}
261	698	698	{dA}{dV}{dG}{dV}{dE}{dG}
262	699	699	{dY}{dV}{dG}{dV}{dE}{dG}
263	700	700	{dC}{dV}{dG}{dV}{dE}{dG}
264	701	701	{dR}{dA}{dG}{dV}{dE}{dG}
265	702	702	{dR}{dI}{dG}{dV}{dE}{dG}
266	703	703	{dR}{dT}{dG}{dV}{dE}{dG}
267	704	704	{dR}{dL}{dG}{dV}{dE}{dG}
268	705	705	{dR}{dW}{dG}{dV}{dE}{dG}
269	706	706	{dR}{dC}{dG}{dV}{dE}{dG}
270	707	707	{dR}{dF}{dG}{dV}{dE}{dG}
271	708	708	{dR}{dQ}{dG}{dV}{dE}{dG}
272	709	709	{dP}{dA}{dQ}{dR}{dV}
273	710	710	{dP}{dA}{dQ}{dV}{dR}
274	711	711	{dP}{dA}{dR}{dQ}{dV}
275	712	712	{dP}{dQ}{dA}{dR}{dV}
276	713	713	{dA}{dP}{dQ}{dR}{dV}
277	714	714	{dP}{dA}{dQ}{dK}{dV}
278	715	715	{dP}{dA}{dQ}{dA}{dV}
279	716	716	{dP}{dA}{dQ}{dG}{dV}
280	717	717	{dP}{dA}{dQ}{dP}{dV}
281	718	718	{dP}{dA}{dQ}{dR}{dA}
282	719	719	{dP}{dA}{dQ}{dR}{dI}
283	720	720	{dP}{dA}{dQ}{dR}{dT}
284	721	721	{dP}{dA}{dQ}{dR}{dL}
285	722	722	{dP}{dA}{dQ}{dR}{dW}
286	723	723	{dP}{dA}{dQ}{dR}{dC}
287	724	724	{dP}{dA}{dQ}{dR}{dF}
288	725	725	{dP}{dA}{dQ}{dR}{dQ}
289	726	726	{dP}{dA}{dQ}{dR}{dH}
290	727	727	{dP}{dA}{dQ}{dR}{dP}
291	728	728	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
292	729	729	{dS}{dA}{dA}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
293	730	730	{dS}{dA}{dN}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
294	731	731	{dS}{dA}{dD}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
295	732	732	{dS}{dA}{dC}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
296	733	733	{dS}{dA}{dH}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
297	734	734	{dS}{dA}{dY}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dG}{dY}{dS}{dD}
298	735	735	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dK}{dY}{dS}{dD}
299	736	736	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dA}{dY}{dS}{dD}
300	737	737	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dN}{dY}{dS}{dD}
301	738	738	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dD}{dY}{dS}{dD}
302	739	739	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dV}{dY}{dS}{dD}
303	740	740	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dH}{dY}{dS}{dD}
304	741	741	{dS}{dA}{dK}{dS}{dP}{dF}{dP}{dA}{dQ}{dR}{dV}{dG}{dV}{dE}{dY}{dY}{dS}{dD}
305	742	742	{dD}{dS}{dY}{GEVGVQRQAPF}{dP}{dS}{dR}{dA}{dS}
306	743	743	{dD}{dS}{dY}{dG}{dE}{dV}{dG}{dV}{dR}{dQ}{dA}{dP}{dF}
307	744	744	{dD}{dS}{dY}{dG}{dE}{dV}{dG}{dV}{dR}{dQ}{dA}{dP}{dF}{dP}{dS}
308	745	745	{dG}{dE}{dV}{dG}{dV}{dR}{dQ}{dA}{dP}{dF}{dP}{dS}{dR}{dA}{dS}
309	746	746	GEVGVQRQAPF{dP}{dS}{dR}{dA}{dS}
310	747	747	GEVGVQRQAP
311	748	748	GVVRQAP
312	749	749	GVVRQAP
313	750	750	VRQA
314	751	751	GEVGVVRQ
315	752	752	GEVGVVR

In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 438-752. In some embodiments, the present invention provides a peptide comprising the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 438-752 wherein the peptide has delta opioid agonist activity.

In some embodiments, a retro-inverso variant as described in this section has delta opioid agonist activity. In some embodiments, a retro-inverso variant as described in this section has analgesic efficacy in a rodent model of pain as described in Example 5.

2.9. Variant Peptides

5 In some embodiments, the present invention provides “variant” peptides that differ from, or that comprise a peptide that differs from, any one or PEP NOs: and/or SEQ ID NOs: 1-315 or 438-752 – as described in more detail below. Similarly, in some embodiments, the present invention provides variant peptides that differ from, or that comprise a peptide that differs from, the consensus sequences of PEP NOs: and/or SEQ ID NOs: 316, 317, or 318-437, or 753-875 – as
10 described in more detail below. In some embodiments, such variant peptides have delta opioid agonist activity. One of ordinary skill in the art can readily determine if any given variant peptide has delta opioid agonist activity using any suitable method known in the art or the methods described in the Examples section of this patent disclosure.

The differences between the “variant” peptides provided herein and peptides that comprise PEP
15 NOs: and/or SEQ ID NOs: 1-315 (or PEP NOs: and/or SEQ ID NOs: 316-875) can occur at various levels, including at the level of the amino acid residues (e.g., variant peptides may comprise amino acid substitutions, deletions, or additions as compared to PEP NOs: and/or SEQ ID NOs: 1-315 (or PEP NOs: and/or SEQ ID NOs: 316-875)), at the level of amino acid modifications (e.g., variant peptides may have modifications added or removed as compared to PEP NOs: and/or SEQ
20 ID NOs: 1-315 (or PEP NOs: and/or SEQ ID NOs: 316-875), or may include different modifications from those in PEP NOs: and/or SEQ ID NOs: 1-315 (or PEP NOs: and/or SEQ ID NOs: 316-875)), and at the level of other peptide attributes (such as cyclization, dimerization, multimerization, and the like).

In some embodiments, a variant peptide described in this section and its subsections has delta
25 opioid agonist activity. In some embodiments, a variant peptide described in this section and its subsections has analgesic efficacy in a rodent model of pain as described in Example 5.

Examples of variant peptides provided by the present invention are described in more detail below.

2.9.1. Deletion Variants

In some embodiments, the present invention provides a variant peptide that contains one or more
30 amino acid deletions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a variant peptide that contains one or more amino acid deletions as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs:

753-875. In some embodiments, one or more of the deletions is internal. In some embodiments, one or more of the deletions is at the N and/or C terminus.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NO: and/or SEQ ID NO: 1-875, wherein one position is deleted and, to the extent that the
5 deletion is not located at the N-or C-terminus of the peptide, the two amino acids flanking the deletion are linked by a peptide bond.

In some embodiments, the present invention provides a variant peptide that contains one or more amino acid deletions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some
10 embodiments, the present invention provides a variant peptide that contains one or more amino acid deletions as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. In some embodiments, one or more of the deletions is internal. In some embodiments, one or more of the deletions is at the N and/or C terminus.

In some embodiments, the present invention provides variant peptides that differ from any of PEP
15 NO: and/or SEQ ID NO: 1-875, wherein up to two sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NO: and/or SEQ ID NO: 1-875, wherein up to three sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

20 In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein one position is deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to two sequential or non-sequential positions are
25 deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to three sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP
30 NOs: and/or SEQ ID NOs: 1-875, wherein up to four sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to five sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

5 In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to six sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to seven sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

10 In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to eight sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein up to nine sequential or non-sequential positions are
15 deleted and the preceding and subsequent positions are linked by a peptide bond.

In some embodiments, the present invention provides variant peptides that differ from any of PEP NOs: and/or SEQ ID NOs: 1-875, wherein ten or more sequential or non-sequential positions are deleted and the preceding and subsequent positions are linked by a peptide bond.

2.9.2. Fragment Variants

20 In some embodiments, the present invention provides variant peptides that are fragments of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 2-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 3-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present
25 invention provides variant peptides comprising amino acid residues 4-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 5-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 6-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention
30 provides variant peptides comprising amino acid residues 7-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 8-10 of any of PEP NOs: and/or SEQ ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 2-11 of any of PEP

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ID NOs: 1-875. In some embodiments, the present invention provides variant peptides comprising amino acid residues 10-20 of any of PEP NOs: and/or SEQ ID NOs: 1-875.

2.9.3. Addition Variants

In some embodiments, the present invention provides a variant peptide that contains one or more amino acid insertions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a variant peptide that contains one or more amino acid insertions as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. In some embodiments, one or more of the insertions is internal. In some embodiments, one or more of the insertions is at the N and/or C terminus.

In some embodiments, the present invention provides a variant peptide comprising the amino acid sequence of any of PEP NO: and/or SEQ ID NO: 1-875, and further comprising at its N-terminus amino acids, or an amino acid sequence, selected from: RR, RRRR (PEP NO: and/or SEQ ID NO: 876), RG, SC, or SRASC (PEP NO: and/or SEQ ID NO: 877) wherein the variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides a variant peptide comprising the amino acid sequence of any of PEP NO: and/or SEQ ID NO: 1-875, and further comprising at its C-terminus amino acids, or an amino acid sequence, selected from: C, CN, CRR, CRRRR (PEP NO: and/or SEQ ID NO: 878), CDSY (PEP NO: and/or SEQ ID NO: 879), CDSYGEVGV (PEP NO: and/or SEQ ID NO: 880), and K wherein the variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-875 having additional 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or more amino acids at the N-terminal and/or C-terminal end wherein the variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-875 having additional 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17 amino acids at the N-terminal and/or C-terminal end wherein the variant peptide has delta opioid agonist activity. In some embodiments, the present invention provides peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-875 having additional 18-30 amino acids at the N-terminal and/or C-terminal end wherein the variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-875 having additional more than 30 amino acids at the N-terminal and/or C-terminal end wherein the variant peptide has delta opioid agonist activity.

In some embodiments, the present invention provides a variant peptide that contains one or more amino acid insertions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a variant peptide that contains one or more amino acid insertions as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. In some embodiments, one or more of the insertions is internal. In some embodiments, one or more of the insertions is at the N and/or C terminus.

2.9.4.Substitution Variants

In some embodiments, the present invention provides a variant peptide that contains one or more amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a variant peptide that contains one or more amino acid substitutions as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. In some embodiments, a substitution replaces an amino acid with a similar or homologous amino acid. In some embodiments, a substitution replaces an amino acid with a dissimilar amino acid. In some embodiments, the substitution is a conservative substitution having little or no effect on the charge, polarity, or hydrophobicity of the peptide. In some embodiments, the substitution is a non-conservative substitution that changes the charge, polarity, or hydrophobicity of the peptide.

In some embodiments, the present invention provides a variant peptide that contains 1 amino acid substitution as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a variant peptide that contains 2 amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a variant peptide that contains 3 amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a variant peptide that contains 4 amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or

SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a variant peptide that contains 5 amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or
5 SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a variant peptide that contains 6 amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or
10 SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a variant peptide that contains 7 or more amino acid substitutions as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315, or PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

15 In some embodiments, a substitution replaces an amino acid with a similar or homologous amino acid. In some embodiments, a substitution replaces an amino acid with a dissimilar amino acid. In some embodiments, the substitution is a conservative substitution having little or no effect on the charge, polarity, or hydrophobicity of the peptide. In some embodiments, the substitution is a non-conservative substitution that changes the charge, polarity, or hydrophobicity of the peptide.

20 **2.9.5. Percent Identity Variants**

In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 40% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 50% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315. In some
25 embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 60% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 70% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence
30 that has at least 80% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 90% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315. In some

embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 95% identity to any of PEP NOs: and/or SEQ ID NOs: 1-315.

In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 40% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632. In some
5 embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 50% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 60% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632. In some
10 embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 70% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 80% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632. In some
15 embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 90% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632. In some embodiments, the present invention provides variant peptides comprising an amino acid sequence that has at least 95% identity to any of PEP NOs: and/or SEQ ID NOs: 318-632.

2.9.6. Activity Variants and Groups

In some embodiments, the present invention provides peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-315 having up to 5 amino acid residues substituted, added or deleted
20 as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-315 having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides isolated peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-315 having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some
25 embodiments, the present invention provides isolated peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-315 having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides isolated peptides that are variants of any of PEP NOs: and/or SEQ ID NOs: 1-315 having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some such embodiments (i.e., whether there
30 are 5, 4, 3, 2, or 1 amino acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5A.

In some embodiments, the present invention provides peptides comprising or consisting of variants of any of PEP NOs: and/or SEQ ID NOs: 1-304 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or

X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5A.

Table 5A. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F).

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, {n-peg40k-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, A, D, F, G, K, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, A, C, D, G, H, K, N, S, Y
X ₆	deletion, {dE}, {n-pal-A}, {n-pal-E}, {βE}, {βhE}, A, D, E, G, I, K, L, Q, V
X ₇	deletion, {n-pal-V}, {βhV}, A, E, G, I, L, M, V, W
X ₈	deletion, {n-pal-G}, A, D, G, S, V
X ₉	deletion, {dV}, {n-pal-A}, {n-pal-C}, {n-pal-F}, {n-pal-H}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-Q}, {n-pal-R}, {n-pal-T}, {n-pal-V}, {n-pal-W}, {βhV}, A, C, F, I, K, L, Q
X ₁₀	deletion, {hR}, {n-pal-R}, A, C, D, E, G, H, K, P, Q, R, V, W, Y
X ₁₁	deletion, {n-pal-Q}, {βhQ}, A, E, H, N, Q, R
X ₁₂	deletion, {c-amid-A}, {βA}, {βhA}, A, G, L, P, Q, T, V
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, {hP}, {βhP}, A, K, P, S
X ₁₄	deletion, {c-amid-F}, {dF}, {hF}, {βhF}, A, F, I, K, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {{r-peg40k-dbcO}-{azide-K}}, {r-ste-K}, A, C, D, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CDSY (PEP NO: and/or SEQ ID NO: 879), CDSYGEVGV (PEP NO: and/or SEQ ID NO: 880), CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

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In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 1A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 1A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 1A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 1A having up to 2 amino acid residues substituted, added or deleted as compared thereto.

In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 1A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5B. In some embodiments, the present Invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 1 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or

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X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5B.

Table 5B. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of

5 **Fig. 1A-F)** for the set of peptides in Group 1.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, {n-peg40k-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, A, D, F, G, K, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, A, C, D, G, H, K, N, S, Y
X ₆	deletion, {dE}, {n-pal-A}, {n-pal-E}, {βE}, {βhE}, A, D, E, G, I, K, L, Q, V
X ₇	deletion, {n-pal-V}, A, E, I, L, M, V, W
X ₈	deletion, {n-pal-G}, A, D, G, S
X ₉	deletion, {dV}, {n-pal-A}, {n-pal-C}, {n-pal-H}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-Q}, {n-pal-R}, {n-pal-T}, {n-pal-V}, {n-pal-W}, {βhV}, A, C, F, I, K, L, Q, T
X ₁₀	deletion, {hR}, {n-pal-R}, A, C, E, G, K, P, R, V, W
X ₁₁	deletion, A, H, N, Q
X ₁₂	deletion, {c-amid-A}, {βA}, {βhA}, A, G, P, Q, T, V
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, {hP}, {βhP}, A, P, S
X ₁₄	deletion, {c-amid-F}, {dF}, {hF}, {βhF}, A, F, I, K, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {r-peg40k-dbcO}-{azide-K}, {r-ste-K}, A, C, D, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CDSY (PEP NO: and/or SEQ ID NO: 879), CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 2A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 2A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 2A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 2A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 2A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5C. In some embodiments, the present Invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in

Group 2 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5C.

- 5 **Table 5C.** Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 2.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, {n-peg40k-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, A, D, F, G, K, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, A, C, D, G, H, K, N, S, Y
X ₆	deletion, {dE}, {n-pal-A}, {n-pal-E}, {βE}, {βhE}, D, E, G, I, K, L, Q
X ₇	deletion, {n-pal-V}, A, I, L, M, V, W
X ₈	deletion, {n-pal-G}, A, D, G, S
X ₉	deletion, {n-pal-A}, {n-pal-C}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-R}, {n-pal-T}, {n-pal-V}, {n-pal-W}, {βhV}, A, C, F, I, L, V, W
X ₁₀	deletion, {hR}, {n-pal-R}, A, C, E, K, P, R, V, W
X ₁₁	deletion, A, H, N, Q
X ₁₂	deletion, {c-amid-A}, {βA}, {βhA}, A, G, P, Q, T
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, {hP}, {βhP}, A, P, S
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, A, F, I, K, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	Deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {{r-peg40k-dbo}-{azide-K}}, {r-ste-K}, A, C, D, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CDSY (PEP NO: and/or SEQ ID NO: 879), CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 3A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 3A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 3A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 3A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 3A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5D. In some embodiments, the present Invention

provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 3 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5D.

Table 5D. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 3.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg40k-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, A, D, F, G, K, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, A, C, D, G, H, S, Y
X ₆	deletion, {dE}, {n-pal-A}, {n-pal-E}, {βE}, {βhE}, D, E, G, I, K, L, Q, V
X ₇	deletion, {n-pal-V}, A, E, I, L, M, V, W
X ₈	deletion, {n-pal-G}, A, D, G, S
X ₉	deletion, {n-pal-A}, {n-pal-C}, {n-pal-H}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-Q}, {n-pal-R}, {n-pal-T}, {n-pal-V}, {n-pal-W}, {βhV}, A, C, F, I, L, Q, T, V, W
X ₁₀	deletion, {hR}, K, P, R, V
X ₁₁	deletion, A, H, N, Q
X ₁₂	deletion, {c-amid-A}, {βA}, A, G, P, Q, V
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, {hP}, {βhP}, A, P
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, A, F, I, K, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {{r-peg40k-dbo}-{azide-K}}, {r-ste-K}, A, C, D, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CDSY (PEP NO: and/or SEQ ID NO: 879), CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 4A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 4A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 4A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 4A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 4A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are

selected from among those listed in Table 5E. In some embodiments, the present Invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 4 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5E.

Table 5E. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 4.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, A, D, F, K, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, G, Y
X ₆	deletion, {n-pal-A}, {n-pal-E}, {βE}, {βhE}, D, E, G, I, K, L, Q, V
X ₇	deletion, {n-pal-V}, A, E, I, L, M, V, W
X ₈	deletion, {n-pal-G}, A, D, G
X ₉	deletion, {n-pal-A}, {n-pal-C}, {n-pal-H}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-Q}, {n-pal-R}, {n-pal-T}, {n-pal-V}, A, F, I, T, V, W
X ₁₀	{hR}, K, R, V
X ₁₁	deletion, A, H, N, Q
X ₁₂	deletion, {c-amid-A}, {βA}, A, G
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, {hP}, {βhP}, P
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, A, F, I, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {{r-peg40k-dbcO}-{azide-K}}, {r-ste-K}, A, C, D, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 5A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 5A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 5A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 5A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 5A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino

acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5F. In some embodiments, the present Invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 5 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5F.

Table 5F. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 5.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, D, F, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, G
X ₆	deletion, {n-pal-A}, {n-pal-E}, {βE}, D, E, G, I, Q
X ₇	deletion, A, I, V, W
X ₈	deletion, {n-pal-G}, A, G
X ₉	deletion, {n-pal-C}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-V}, A, I, V, W
X ₁₀	{hR}, K, R
X ₁₁	deletion, A, H, Q
X ₁₂	deletion, {c-amid-A}, A, G
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, P
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, A, F, I, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {{r-peg40k-dbcO}-{azide-K}}, {r-ste-K}, A, C, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

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In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 6A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 6A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 6A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 6A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 6A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino

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acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5G. In some embodiments, the present Invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 6 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5G.

Table 5G. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 6.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, D, F, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, G
X ₆	deletion, {n-pal-A}, {n-pal-E}, D, E, G, I, L, Q
X ₇	deletion, {n-pal-V}, A, I, M, V, W
X ₈	deletion, {n-pal-G}, A, D, G
X ₉	deletion, {n-pal-C}, {n-pal-H}, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-Q}, {n-pal-V}, {n-pal-W}, A, F, I, V, W
X ₁₀	{hR}, K, R
X ₁₁	deletion, A, H, Q
X ₁₂	deletion, {c-amid-A}, A, G
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, P
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, A, F, I, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, L, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {{r-peg40k-dbcO}-{azide-K}}, {r-ste-K}, A, H, K, N, Q, R, S, Y
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, G, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, D, F, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CDSY (PEP NO: and/or SEQ ID NO: 879), CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

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In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 7A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 7A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides isolated peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 7A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 7A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 7A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether

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there are 5, 4, 3, 2, or 1 amino acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5H. In some embodiments, the present invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 7 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5H.

Table 5H. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 7.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {dβD}, {htt-cyclic-D}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, {n-peg12-{dβD}}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, D, F, W, Y
X ₅	deletion, {n-pal-E}, {n-pal-G}, G
X ₆	deletion, {n-pal-A}, {n-pal-E}, E, G, I, Q
X ₇	deletion, A, I, V, W
X ₈	deletion, {n-pal-G}, A, G
X ₉	deletion, {n-pal-I}, {n-pal-L}, {n-pal-P}, {n-pal-V}, A, V, W
X ₁₀	{hR}, K, R
X ₁₁	deletion, A, H, Q
X ₁₂	deletion, {c-amid-A}, A, G
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, P
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, F, I, L, Y
X ₁₅	deletion, {c-amid-P}, {dP}, K, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {r-ste-K}, K, R, S
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-{r-peg40k-{dC}}}, {c-amid-C}, {dC}, C, C{c-amid-N}, CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

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In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 8A having up to 5 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 8A having up to 4 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any PEP NO: and/or SEQ ID NO: in Group 8A having up to 3 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 8A having up to 2 amino acid residues substituted, added or deleted as compared thereto. In some embodiments, the present invention provides peptides that are variants of any of PEP NO: and/or SEQ ID NO: in Group 8A having up to 1 amino acid residues substituted, added or deleted as compared thereto. In some of such embodiments (i.e., whether there are 5, 4, 3, 2, or 1 amino

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acid residues substituted, added or deleted), the amino acid substitutions, additions or deletions are selected from among those listed in Table 5I. In some embodiments, the present Invention provides peptides comprising or consisting of variants of any PEP NO: and/or SEQ ID NO: in Group 8 that contain any one or more of the amino acid variations at residues X₁, and/or X₂, and/or X₃, and/or X₄, and/or X₅, and/or X₆, and/or X₇, and/or X₈, and/or X₉, and/or X₁₀, and/or X₁₁, and/or X₁₂, and/or X₁₃, and/or X₁₄, and/or X₁₅, and/or X₁₆, and/or X₁₇, and/or X₁₈, and/or X₁₉, and/or X₂₀ that are set forth in Table 5I.

Table 5I. Examples of amino acid variations at positions X₁ through X₂₀ (using numbering of Fig. 1A-F) for the set of peptides in Group 8.

Amino Acid Position	Amino acid variations
X ₁	deletion, {n-acet-R}R, {n-acet-R}RRR (PEP NO: and/or SEQ ID NO: 881), RG, SC, SRASC (PEP NO: and/or SEQ ID NO: 877)
X ₂	deletion, {dD}, {n-acet-{dD}}, {n-acet-{dβD}}, {n-acet-D}, {n-pal-D}, D, K, R
X ₃	deletion, {dS}, {n-acet-{dS}}, G, K, S, W
X ₄	deletion, {DMT}, {dY}, {n-acet-Y}, {n-pal-{dY}}, {n-pal-Y}, D, F, Y
X ₅	deletion, {n-pal-G}, G
X ₆	deletion, {n-pal-A}, {n-pal-E}, E
X ₇	deletion, A, V
X ₈	deletion, A, G
X ₉	{n-pal-I}, {n-pal-L}, {n-pal-V}, A, V
X ₁₀	{hR}, K, R
X ₁₁	deletion, A, H, Q
X ₁₂	deletion, {c-amid-A}, A, G
X ₁₃	deletion, {c-amid-A}, {c-amid-P}, P
X ₁₄	deletion, {c-amid-F}, {hF}, {βhF}, F, I, Y
X ₁₅	deletion, {c-amid-P}, {dP}, P, V
X ₁₆	deletion, {dS}, A, K, L, P, S
X ₁₇	deletion, {c-amid-{r-pal-K}}, {c-amid-R}, {dK}, {dR}, {r-pal-K}, {r-ste-K}, K, R, S
X ₁₈	deletion, {c-amid-{dA}}, {dA}, A, I, K, V
X ₁₉	deletion, {c-amid-{dS}}, {c-amid-S}, {dS}, A, K, S
X ₂₀	deletion, {c-amid-{dC}}, {c-amid-C}, C, C{c-amid-N}, CN, CR{c-amid-R}, CRRR{c-amid-R} (PEP NO: and/or SEQ ID NO: 882), K

2.9.7. Modification Variants

In some embodiments, the present invention provides a variant peptide that has a modified N-terminus and/or a modified C-terminus as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a variant peptide that has a modified N-terminus and/or a modified C-terminus as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. For example, in some embodiments, variant peptides may comprise an N-terminal acetyl group, polyethylene glycol (peg) group, or palmitoyl group. Similarly, in some embodiments, variant peptides may comprise an N-terminal amide group, azide group, palmitoyl group, or palmitoyl group. Other examples of N-terminal and/or C-terminal groups that can be used include hydrophobic groups, such as a linear or cyclic C2-C18 aliphatic

or aromatic hydrocarbon, a naphthyl group, a phenyl group, an octanoyl group, and a valeryl group, including an isovaleryl group.

In some embodiments, the present invention provides a variant peptide that has been modified as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315 to incorporate a tag or label, such as for use in purification or detection. In some embodiments, the present invention provides a variant peptide that has been modified as compared to any one of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. Non-limiting examples of such tags and labels include FLAG tags, HA tags, His tags, Myc tags, GST tags, fluorescent labels, isotopic labels, and the like.

In some embodiments, the present invention provides a peptide comprising a variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315 containing one more amino acid modifications, or containing one or more amino acid modifications that differ from those in any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a peptide comprising a variant PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875 containing one more amino acid modifications, or containing one or more amino acid modifications that differ from those in PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. In some embodiments, the modification is a change of the chirality of an amino acid from the L- to D-form. In some embodiments, the modification is a change of the chirality of an amino acid from the D- to L-form. In some embodiments, the modification is a change of an amino acid to its alpha form to its beta form. In some embodiments, the modification is a change of an amino acid to its beta form to its alpha form. In some embodiments, the modification is a change of an amino acid to its homo form. In some embodiments, the modification is acetylation or deacetylation of an amino acid. In some embodiments, the modification is amidation or deamidation of an amino acid. In some embodiments, the modification is palmitoylation or depalmitoylation of an amino acid. In some embodiments, the modification is conjugation of stearic acid to an amino acid or removal of stearic acid from an amino acid. In some embodiments, the modification is the conjugation of any fatty acid to an amino acid or removal of any fatty acid from an amino acid. In some embodiments, the modification is conjugation of polyethylene glycol (PEG) to an amino acid or removal of PEG from an amino acid. Other suitable amino acid modifications that can be included are described elsewhere herein, including in the "Definitions" section above and in other sections below.

In some embodiments, the present invention provides a branched variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a branched variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

- 5 In some embodiments, the present invention provides a cyclized variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a cyclized variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

- 10 In some embodiments, the present invention provides a dimerized variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a dimerized variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

- 15 In some embodiments, the present invention provides a multimerized variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a multimerized variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

- 20 In some embodiments, the variant peptides described herein can be provided having unmodified amino acids, modified amino acids, or a combination of both modified and unmodified amino acids. Wherever a peptide is illustrated herein as containing unmodified amino acids, a variant of that peptide in which one or more of the unmodified amino acids is replaced with a modified version of that amino acid, is also provided. Conversely, wherever a peptide is illustrated herein as containing modified amino acids, a variant version of that peptide in which one or more of the modified amino acids is replaced with an unmodified version of that amino acid, or replaced with
- 25 a different modified version of that amino acid, is also provided. Any suitable modified amino acids known in the art can be used. Examples of modified amino acids that can be used include, but are not limited to, amino acids having D chirality as opposed to their natural L chirality, amino acids in their beta form as opposed to their alpha form, homo amino acids (e.g., homoalanine), beta homo amino acids, N-methyl amino acids, alpha-methyl amino acids, amino acids that are
- 30 acetylated, amino acids that are amidated, amino acids that are palmitoylated, amino acids that are phosphorylated, amino acids that are glycosylated, amino acids that have undergone stearic acid conjugation, amino acids that are pegylated, amino acids that have been labelled or tagged (e.g. using a fluorescent or isotopic label or tag), amino acids that have an added protecting group, and amino acids altered using other manipulations or modifications known in the art.

Similarly, in some embodiments, the variant peptides described herein can be modified at the peptide level (or described in terms of their modification at the peptide level). For example, wherever a specific peptide is illustrated herein, a variant version of that peptide containing one or more peptide modifications is provided. Examples of such peptide modifications include
5 acetylation, amidation, palmitoylation, phosphorylation, glycosylation, stearic acid conjugation, pegylation, cyclization, dimerization, multimerization, conjugation to a label or tag (e.g., a fluorescent or isotopic label or tag), addition of a protecting group, and other peptide modifications known in the art.

In some embodiments, the present invention provides a variant peptide that has a modified N-terminus and/or a modified C-terminus as compared to any one of PEP NOs: and/or SEQ ID NOs:
10 1-315. In some embodiments, the present invention provides a variant peptide that has a modified N-terminus and/or a modified C-terminus as compared to PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. For example, in some embodiments, variant peptides
15 may comprise an N-terminal acetyl group, polyethylene glycol (peg) group, or palmitoyl group. Similarly, in some embodiments, variant peptides may comprise an N-terminal amide group, azide group, palmitoyl group, or palmitoyl group. Other examples of N-terminal and/or C-terminal groups that can be used include hydrophobic groups, such as a linear or cyclic C2-C18 aliphatic or aromatic hydrocarbon, a naphthyl group, a phenyl group, an octanoyl group, and a valeryl group,
20 including an isovaleryl group.

In some embodiments, the present invention provides a variant peptide that has been modified as compared to any one of PEP NOs: and/or SEQ ID NOs: 1-315 to incorporate a tag or label, such as for use in purification or detection. In some embodiments, the present invention provides a variant peptide that has been modified as compared to any one of PEP NOs: and/or SEQ ID NOs:
25 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. Non-limiting examples of such tags and labels include FLAG tags, HA tags, His tags, Myc tags, GST tags, fluorescent labels, isotopic labels, and the like.

In some embodiments, the present invention provides a peptide comprising a variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315 containing one more amino acid modifications, or
30 containing one or more amino acid modifications that differ from those in any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a peptide comprising a variant PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875 containing one more amino acid modifications, or containing one or more amino acid

modifications that differ from those in PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875. In some embodiments, the modification is a change of the chirality of an amino acid from the L- to D-form. In some embodiments, the modification is a change of the
5 chirality of an amino acid from the D- to L-form. In some embodiments, the modification is a change of an amino acid to its alpha form to its beta form. In some embodiments, the modification is a change of an amino acid to its beta form to its alpha form. In some embodiments, the modification is a change of an amino acid to its homo form. In some embodiments, the modification is acetylation or deacetylation of an amino acid. In some embodiments, the
10 modification is amidation or deamidation of an amino acid. In some embodiments, the modification is palmitoylation or depalmitoylation of an amino acid. In some embodiments, the modification is conjugation of stearic acid to an amino acid or removal of stearic acid from an amino acid. In some embodiments, the modification is the conjugation of any fatty acid to an amino acid or removal of any fatty acid from an amino acid. In some embodiments, the
15 modification is conjugation of polyethylene glycol (PEG) to an amino acid or removal of PEG from an amino acid. Other suitable amino acid modifications that can be included are described elsewhere herein, including in the “Definitions” section above and in other sections below.

In some embodiments, the present invention provides a branched variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a branched
20 variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a cyclized variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a cyclized
25 variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the present invention provides a dimerized variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a dimerized
variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

30 In some embodiments, the present invention provides a multimerized variant of any one of PEP NOs: and/or SEQ ID NOs: 1-315. In some embodiments, the present invention provides a multimerized variant of PEP NOs: and/or SEQ ID NOs: 316-317, or PEP NOs: and/or SEQ ID NOs: 318-437 or PEP NOs: and/or SEQ ID NOs: 438-752 or PEP NOs: and/or SEQ ID NOs: 753-875.

In some embodiments, the variant peptides described herein can be provided having unmodified amino acids, modified amino acids, or a combination of both modified and unmodified amino acids. Wherever a peptide is illustrated herein as containing unmodified amino acids, a variant of that peptide in which one or more of the unmodified amino acids is replaced with a modified version of that amino acid, is also provided. Conversely, wherever a peptide is illustrated herein as containing modified amino acids, a variant version of that peptide in which one or more of the modified amino acids is replaced with an unmodified version of that amino acid, or replaced with a different modified version of that amino acid, is also provided. Any suitable modified amino acids known in the art can be used. Examples of modified amino acids that can be used include, but are not limited to, amino acids having D chirality as opposed to L chirality, amino acids in their beta form as opposed to their alpha form, homo amino acids (e.g., homoalanine), beta homo amino acids, N-methyl amino acids, alpha-methyl amino acids, amino acids that are acetylated, amino acids that are amidated, amino acids that are palmitoylated, amino acids that are phosphorylated, amino acids that are glycosylated, amino acids that have undergone stearic acid conjugation, amino acids that are pegylated, amino acids that have been labelled or tagged (e.g. using a fluorescent or isotopic label or tag), amino acids that have an added protecting group, and amino acids altered using other manipulations or modifications known in the art.

Similarly, in some embodiments, the variant peptides described herein can be modified at the peptide level (or described in terms of their modification at the peptide level). For example, wherever a specific peptide is illustrated herein, a variant version of that peptide containing one or more peptide modifications is provided. Examples of such peptide modifications include acetylation, amidation, palmitoylation, phosphorylation, glycosylation, stearic acid conjugation, pegylation, cyclization, dimerization, multimerization, conjugation to a label or tag (e.g., a fluorescent or isotopic label or tag), addition of a protecting group, and other peptide modifications known in the art.

In embodiments of the present invention that refer to amino acid substitutions, in some embodiments, any possible amino acid substitution can be made including but not limited to substituting an amino acid for any suitable canonical amino acid, non-canonical amino acid, naturally occurring amino acid, non-naturally occurring amino acid, synthetic amino acid, modified amino acid, or amino acid analogue known in the art. In some embodiments, amino acids are substituted with others having one or more similar properties (such as polarity, charge, or size). In some embodiments, substitutions of an amino acid may be made with other members of the class to which the amino acid to be replaced belongs. For example, the nonpolar amino acids include glycine, alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and

methionine. The polar neutral amino acids include serine, threonine, cysteine, tyrosine, asparagine, and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid. Substitutions of a nonpolar amino acid for another nonpolar amino acid, or of a polar
5 neutral amino acid for another polar neutral amino acid, or of a positively charged (basic) amino acid for another positively charged (basic) amino acid, or of a negatively charged (acidic) amino acid for another negatively charged (acidic) amino acid, are generally understood to be conservative substitutions. Examples of modified amino acids that can be used include amino acids having D chirality as opposed to L chirality, amino acids in their beta form as opposed to
10 their alpha form, homo amino acids (e.g., homoalanine), gamma amino acids, beta homo amino acids, N-methyl amino acids, alpha-methyl amino acids, beta-methyl amino acids, fluoro-amino acids, amino acids that are acetylated, amino acids that are amidated, amino acids that are phosphorylated, amino acids that are palmitoylated, amino acids that are glycosylated, amino acids that have undergone stearic acid conjugation, amino acids that are pegylated, amino acids
15 that have been labelled or tagged (e.g. using a fluorescent or isotopic label or tag), amino acids that have an added protecting group, and amino acids modified using other manipulations or modifications known in the art.

In some embodiments, either D or L enantiomers of amino acids can be used in the variant peptides provided herein.

20 In some embodiments, the variant peptides provided herein may contain a “D-amino acid” or a “β-amino acid” or a “D-β-amino acid” in place of an “L” amino acid at one or more amino acid positions of any of the sequences provided herein. In some embodiments, the variant peptides provided herein may contain a “gamma amino acid” or other amino acid side chain modifications known in the art.

25 In some embodiments, the variant peptides of the invention may contain an amino acid modification at any one or more amino acid positions in any of the amino acid sequences provided herein. Examples of such amino acid modifications include, but are not limited to, amino acids having D chirality as opposed to L chirality, amino acids in their beta form as opposed to their alpha form, homo amino acids (e.g., homoalanine), gamma amino acids, beta homo amino acids,
30 N-methyl amino acids, alpha-methyl amino acids, beta-methyl amino acids, fluoro-amino acids, amino acids that are acetylated, amino acids that are acylated, amino acids that are fatty acylated, amino acids that are amidated, amino acids that are methylated, amino acids that are phosphorylated, amino acids that are palmitoylated, amino acids that are glycosylated, amino acids that have undergone stearic acid conjugation, amino acids that are pegylated, amino acids

conjugated to deoxyribonucleic acids or ribonucleic acids or oligonucleotides or polynucleotides, amino acids that have been labelled or tagged (e.g. using a fluorescent or isotopic label or tag), amino acids that have an added protecting group, and amino acids altered using other manipulations or modifications known in the art.

- 5 In some embodiments, the variant peptides of the invention may be linear peptides. In some embodiments, the variant peptides of the invention may be branched peptides. In some embodiments, the variant peptides of the invention may be cyclized peptides. For example, types of cyclization that may be used include, but are not limited to, amide cyclization from head to tail, amide cyclization to a side chain, ornithine side chain amide cyclization, bicyclization, lassoing, or formation of one, or two, or three, or more disulfide bonds provided. In some embodiments, the variant peptides of the invention may be dimerized. In some embodiments, the variant peptides of the invention may be multimerized. In some embodiments, the variant peptides of the invention may have any other topology known in the art.

In some embodiments, the peptides of the invention may be conjugated to other molecules.

- 15 In some embodiments, the peptides of the invention may be linked to one or more additional moieties to form a single molecule comprising the peptide and the one or more additional moieties, for example at their N-terminal end, C-terminal end, at both ends, or elsewhere in the peptides. Such moieties may include moieties to facilitate and/or improve production, purification, stability in vitro, stability in vivo, affinity, detection, half-life, bioavailability, blood-brain barrier permeation, formulation, affinity or binding to the delta opioid receptor, selectivity for the delta opioid receptor, reduction of undesirable non-delta opioid receptor effects, increase of desirable non-delta opioid receptor effects or any other property that may be useful for a therapeutic peptide. For example, in some embodiments, the peptides described herein may comprise one or more tags useful for detection and/or purification of the peptide.
- 20 Exemplary tags include, but are not limited to, Strep tags, Strep II tags, FLAG tags, glutathione S-transferase (GST) tags, green fluorescent protein (GFP) tags, hemagglutinin A (HA) tags, histidine (His) tags, luciferase tags, maltose-binding protein (MBP) tags, c-Myc tags, protein A tags, protein G tags, and the like. In some embodiments, the peptides described herein may comprise one or more leader sequences, precursor polypeptide sequences, secretion signals, and/or localization signals. In some embodiments, the peptides described herein may be provided in a “pro-drug” form in which the peptide is present within a larger molecule and can be released from the larger molecule (e.g., by enzymatic action or proteolytic cleavage) following administration of the pro-drug to a subject. In each case, additional moieties may be coupled to the peptides described herein using any suitable method including by chemical conjugation or, in

the case of amino acid, peptide, or protein moieties, by expression as a fusion protein. In some embodiments, the peptides described herein may be coupled to additional moieties by use of a linker, such as a peptide “linker” sequence.

In some embodiments, the peptides of the invention are tautomers.

- 5 In some embodiments, the peptides of the invention are isotopically-labeled, for example by inclusion of ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{36}Cl , ^{18}F , ^{123}I , ^{125}I , ^{13}N , ^{15}N , ^{15}O , ^{17}O , ^{18}O , ^{32}P , or ^{35}S . Such isotopically-labeled peptides may be useful in tissue distribution studies. In some embodiments, the peptides of the invention are substituted with heavier isotopes, such as deuterium. In some embodiments, the peptides of the invention are isotopically-labeled by inclusion of one or more
- 10 positron emitting isotopes, such as ^{11}C , ^{18}F , ^{15}O and ^{13}N . Such peptides may be useful in Positron Emission Topography (PET) studies.

3. DOR Binding & Agonist Activity

In some embodiments, the peptides of the present invention bind to a delta opioid receptor (DOR). In some embodiments, the peptides of the present invention bind to a mammalian DOR.

- 15 In some embodiments, the peptides of the present invention bind to a mouse, rat, non-human primate or human DOR. In some embodiments, the peptides of the present invention bind to a human DOR. In some embodiments, the peptides of the present invention bind to the human delta opioid receptor. In some embodiments, the peptides of the present invention bind to the human delta opioid receptor encoded by the nucleotide sequence having the accession number
- 20 NM_000911 (available at https://www.ncbi.nlm.nih.gov/nuccore/NM_000911.4).

In some embodiments, the binding of the peptides of the present invention bind to a DOR is determined using an in vitro binding competitive radioligand assay as described in Example 3.

- In some embodiments, the peptides of the present invention are agonists of a delta opioid receptor (DOR). In some embodiments, the peptides of the present invention are agonists of a
- 25 mammalian delta opioid receptor (DOR). In some embodiments, the peptides of the present invention are agonists of a mouse, rat, non-human primate or human delta opioid receptor (DOR). In some embodiments, the peptides of the present invention are agonists of a human delta opioid receptor (DOR). In some embodiments, the peptides of the present invention are agonists of the human delta opioid receptor. In some embodiments, the peptides of the present
- 30 invention are agonists of the human delta opioid receptor encoded by the nucleotide sequence having the accession number NM_000911 (available at https://www.ncbi.nlm.nih.gov/nuccore/NM_000911.4).

In some embodiments, the DOR agonist activity of the peptides of the present invention is determined by measuring DOR-dependent cAMP production in any suitable in vitro assay known in the art, such as that described in Example 1. In some embodiments, the DOR agonist activity of the peptides of the present invention is determined using any suitable β -Arrestin assay known in the art, such as that described in Example 4 or using a Eurofins DiscoverX PathHunter® β -Arrestin Assay. In some embodiments, the DOR agonist activity of the peptides of the present invention is determined using any suitable in vitro agonist calcium flux assay, such as that described in Example 2 or using a Eurofins DiscoverX ChemiSCREEN™ or ChemiBRITE™ assay. In some embodiments, the DOR agonist activity of the peptides of the present invention is determined using any suitable in vitro receptor internalization assay, such as that described in Example 4 or using a Eurofins DiscoverX PathHunter® Activated GPCR Internalization Assay.

In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 100 μ M in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 10 μ M in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 1 μ M in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 100 nM in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 10 nM in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 1 nM in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 100 pM in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 10 pM in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have an EC₅₀ for agonism of the human delta opioid receptor of < 1 pM in one or more agonist assays as described herein or as is known in the art. In some embodiments, the peptides of the present invention have a gastrointestinal site of action when administered to a subject. In some embodiments, the peptides of the present invention have

a gastrointestinal site of action and do not act on delta opioid receptors in the central nervous system when administered to a subject. In some embodiments, the peptides of the present invention have a gastrointestinal site of action when administered to a subject for the treatment of pain. In some embodiments, the peptides of the present invention have a gastrointestinal site of action and do not act on delta opioid receptors in the central nervous system when administered to a subject for the treatment of pain.

4. Methods of Manufacture

In some embodiments, the peptides described herein can be made by any suitable method known in the art including but not limited to solid phase peptide synthesis, liquid phase peptide synthesis, or, to the extent possible, expression from a nucleic acid molecule encoding a peptide described herein using recombinant methods. Synthesis or expression may be used to produce an entire peptide or one or more fragments of a peptide that are subsequently combined either chemically or enzymatically.

4.1. Manufacture by Recombinant Peptide Expression

To the extent that the peptides of the present invention can be encoded by a nucleic acid molecule (e.g., a DNA or mRNA molecule), the peptides of the present invention can be produced by recombinant peptide expression in any suitable host cell type, including, but not limited to eukaryotic cells, prokaryotic cells, bacteria, mammalian cells, and insect cells. In addition, cell free recombinant peptide expression (also known as in vitro expression) may be used to produce the peptides of the present invention. Methods for recombinant expression of peptides from nucleic acid molecules that encode them are routine and well known in the art, and any suitable methods, vectors, systems, and/or host cell types known in the art can be used. For example, to the extent possible, nucleic acid molecules encoding the peptides described herein can be produced (e.g., by cloning or by chemical synthesis using an oligonucleotide synthesizer), cloned into a suitable expression construct containing a suitable promoter to drive expression, and delivered to host cells (e.g., by transduction or transfection), such that the peptide encoded by the nucleic acid molecules will be expressed by the host cells (by transcription and translation) and can then be purified therefrom. Nucleic acid molecules encoding the peptides of the invention for use in such recombinant peptide expression methods can be designed based on the amino acid sequence of the desired peptide and selection of those codons that encode each amino acid and are favored in the host cell in which the peptide will be expressed. If one or more amino acid or peptide modifications are to be included, such modifications can be added following expression (and optionally purification) of the peptide, for example by chemical and/or enzymatic method. For example, chemical and enzymatic methods for acetylating, amidating, or

pegylating peptides (or specific amino acids within peptides) are well known in the art and can be used to post-translationally modify peptides of the present invention produced by expression.

4.2. Manufacture by Synthesis

The peptides of the present invention can also be chemically synthesized, for example, using
5 solid-phase peptide synthesis or solution-method peptide synthesis. Such methods can be used even for peptides that cannot be encoded by a nucleic acid molecule. Methods for chemically synthesizing peptides are routine and well known in the art. Peptides can be synthesized from amino acids (including non-canonical amino acids and/or modified amino acids) and amino acid analogues that are themselves either synthesized using standard methods known in the art or are
10 obtained from commercial sources. Peptides can be synthesized in linear, branched, or cyclized forms if desired. Further modifications can also be added following synthesis if desired, for example by conjugation of chemical groups by chemical and/or enzymatic method. Methods for chemically synthesizing peptides using solid-phase peptide synthesis or solution-method peptide synthesis are routine and well known in the art. Furthermore, Example 6 of this patent describes
15 synthesis protocols that were used to manufacture several of the peptides described herein.

In some embodiments, where it is desired that a peptide of the present invention contains one or more modified amino acids, a modified amino acid can be used in place of a non-modified version of that amino acid during the initial synthesis of the peptide. In other embodiments, where it is desired that a peptide of the present invention contains one or more modified amino
20 acids, the peptide can initially be synthesized or expressed using non-modified amino acids, which are then modified chemically or enzymatically after the initial synthesis or expression.

In embodiments where the peptides of the present invention are labelled (e.g., isotopically-labeled fluorescently labeled) appropriate labeled amino acids or other labeled reagents can be used in place of the non-labeled amino acids or reagents otherwise employed in the methods of
25 manufacture provided herein. The peptides described herein may be synthesized using techniques and materials described herein and as described, for example, in Fieser and Fieser's Reagents for Organic Synthesis, Volumes 1- 17 (John Wiley and Sons, 1991); Rodd's Chemistry of Carbon Compounds, Volumes 1-5 and Supplemental (Elsevier Science Publishers, 1989); Organic Reactions, Volumes 1-40 (John Wiley and Sons, 1991), Larock's
30 Comprehensive Organic Transformations (VCH Publishers Inc., 1989), March, Advanced Organic Chemistry 4th Ed., (Wiley 1992); Carey and Sundberg, Advanced Organic Chemistry 4th Ed., Vols. A and B (Plenum 2000, 2001), and Green and Wuts, Protective Groups in Organic Synthesis 3rd Ed., (Wiley 1999) (all of which are incorporated by reference for such disclosure).

In some embodiments, the peptides described herein are isolated peptides. In some embodiments, the peptides described herein are not isolated peptides. In some embodiments, the peptides described herein are unpurified. In some other embodiments the peptides described herein are purified, for example to produce the peptide in “substantially pure” form. In such embodiments the peptides may be purified using any suitable method known in the art. Such methods include, but are not limited to, chromatography (e.g., ion exchange, affinity, and/or sizing column chromatography), ammonium sulfate precipitation, centrifugation, differential solubility, or by any other technique for the purification of proteins known to one of ordinary skill in the art. The peptides of the invention may be purified from any source used to produce them including but not limited to synthetic production methods (such as from manufactured vessels, solvents, or other chemicals used or produced as part of production) and, to the extent possible natural production methods (such as cells, proteins, tissues, or organisms). In some embodiments, the purified peptides are provided in a form in which they comprise more than about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95%, 98%, 99%, or 99.9% of the total peptide content of the final composition. In some embodiments, the purified peptides are “substantially pure”.

In some embodiments, the peptides of the present invention may be provided in salt form, for example as a trifluoroacetate (TFA) salt, acetate salt, pamoate salt, chloride salt, sodium salt, or other salt form. In some embodiments, the peptides of the present invention are provided as sodium salts.

In some embodiments, the peptides of the present invention are analyzed following manufacture to confirm successful production, for example using mass spectrometry (MS), liquid chromatography (e.g., HPLC), NMR (e.g., high-resolution multi-dimensional NMR), and the like.

In some embodiments, the peptides of the present invention are analyzed following manufacture to confirm that they have the desired delta opioid receptor agonist activity. Various methods of assessing such activity are known in the art, including those described in the Examples section of this patent disclosure. One such method involves use of an assay in which intracellular cyclic AMP concentrations are modulated by activation of the human delta opioid receptor and measured via luminescence.

5. Nucleic Acid Molecules, Vectors, and Host Cells

In some embodiments, the present invention provides nucleic acid molecules that encode the peptides of the present invention. Similarly, in some embodiments, the present invention

provides vectors that comprise such nucleic acid molecules. Similarly, in some embodiments, the present invention also provides host cells that comprise such nucleic acid molecules or vectors – for example host cells that have been engineered to produce one or more of the peptides of the present invention by recombinant expression.

5 One of ordinary skill in the art can readily determine the nucleotide sequence of a nucleic acid molecule that encodes any one of the peptides described herein – given the universally known and understood nature of the genetic code. Nucleic acid molecules encoding the peptides of the invention can be designed by identifying the codons in the genetic code that encode each amino acid in the desired peptide and, optionally, by selecting those codons that are favored in the host
10 cell in which the peptide will be expressed. In this manner a nucleotide sequence encoding a peptide of the present invention can be determined and a nucleic acid molecule having that nucleotide sequence can be synthetically produced using standard techniques known in the art, such as using an oligonucleotide synthesizer.

In some embodiments, a nucleic acid molecule encoding a peptide of the present invention can
15 be cloned into any suitable vector, such as those to be used for propagation of the nucleic acid molecule or those to be used for expression (i.e., an expression vector) – i.e., to produce the peptide encoded by the nucleic acid molecule by a process of transcription and translation. In embodiments requiring expression, the nucleic acid can be operatively linked to a promoter suitable for directing expression in the desired host cell type, such as a eukaryotic or prokaryotic
20 cell, and may be incorporated into any suitable expression vector.

In some embodiments, nucleic acid molecules encoding the peptides of the present invention can be codon optimized for expression in cells of a particular organism or species.

6. Compositions

In some embodiments, the present invention provides compositions comprising one or more of
25 the peptides described herein, or a salt of any thereof, and one or more additional components. In some embodiments, such compositions may be pharmaceutical compositions.

As used herein the term “salt” refers to both salts of carboxyl groups of the peptides of the present invention and acid addition salts of amino or guanido groups of the peptides of the present invention. Salts of carboxyl groups may be formed by methods known in the art and
30 include inorganic salts, for example sodium, potassium, calcium, ammonium, ferric or zinc salts, and the like, and salts with organic bases such as salts formed for example with amines such as triethanolamine, piperidine, procaine, and the like. Acid addition salts include, for example, salts with mineral acids such as, for example, acetic acid or oxalic acid. Other suitable salts include

but are not limited to trifluoroacetic acid (TFA) salts, sodium salts, magnesium salts, lithium salts, copper salts, manganese salts, aluminum salts, pamoate salts, chloride salts, acetic acid salts, salts derived from non-toxic inorganic or organic acids (such as hydrochloric, phosphoric, acetic, oxalic, tartaric acids), and the like.

5 As used herein, the term “pharmaceutical composition” refers to a composition the components of which permit the biological activity of the active agent(s) (e.g., peptide(s)) contained therein, and that contain no additional components that are unacceptably toxic to a living subject to which the composition may be administered. Thus, the additional components included in pharmaceutical compositions according to the present invention will typically be components
10 known to be safe for administration to human and/or other animal subjects, and/or approved by a regulatory agency of the Federal or a state government, and/or listed in the U.S. Pharmacopeia, and/or other generally recognized pharmacopeia, and/or receiving specific or individual approval from one or more generally recognized regulatory agencies for use in humans and/or other animals. Typically, a pharmaceutical composition according to the present invention will contain
15 an effective amount of a peptide of the invention, preferably in a substantially purified form, together with a suitable amount of one or more pharmaceutically acceptable carriers and/or excipients.

Suitable pharmaceutically acceptable carriers and/or excipients include various diluents and vehicles in which, or with which, the peptides of the present invention can be provided,
20 including, but not limited to, water, aqueous solutions (such as saline solutions, aqueous dextrose solutions, buffers, and the like), organic solvents (such as polyethylene glycols, glycerin, propylene glycol, certain alcohols (such as ethanol) and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil), glycerol, and the like.

25 Additional carriers and/or excipients that can be used include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, wetting agents, emulsifying agents, pH buffering agents, anti-microbial agents, preservatives, and the like.

In some embodiments, the peptides described herein may be provided in a composition (e.g.,
30 pharmaceutical composition) that comprises one or more “additional active agents” (i.e., in addition to the peptide(s) of the present invention and additional components described above). Examples of additional active agents include, but are not limited to agents: (a) that increase an effect produced by a delta opioid agonist peptide of the present invention, (b) that reduce an undesirable side effect of a delta opioid agonist peptide of the present invention, (c) that increase

- a desirable side effect produced by a delta opioid agonist peptide of the present invention, (d) that are useful in the treatment of acute or chronic pain (including but not limited to mu opioid agonists or partial agonists, kappa opioid agonists, acetaminophen, ibuprofen, aspirin, naproxen, gabapentinoids, ketamine, local anesthetics, skeletal muscle relaxants, sodium channel inhibitors, serotonin norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, CGRP inhibitors, and/or DOR agonists or partial agonists), or (e) that are useful in the treatment or prevention of addiction or substance abuse (including but not limited to: mu opioid agonists or partial agonists, mu opioid antagonists, selective serotonin reuptake inhibitors, bupropion, and/or DOR agonists or partial agonists).
- 10 In some embodiments, the present invention provides compositions (e.g., pharmaceutical compositions) that comprise an effective amount of a peptide of the invention. In some embodiments, the present invention provides compositions (e.g., pharmaceutical compositions) that comprise an effective amount of a peptide of the invention in water. In some embodiments, the present invention provides compositions (e.g., pharmaceutical compositions) that comprise an effective amount of a peptide of the invention in water with a flavoring or flavor masking agent. In some embodiments, the present invention provides compositions (e.g., pharmaceutical compositions) that comprise a peptide of the invention in an aqueous solution at a concentration of less than 1 mg/mL, or at least about 1 mg/mL, or at least about 2 mg/mL, or at least about 5 mg/mL, or at least about 10 mg/mL, or at least about 20 mg/mL, or at least about 50 mg/mL, or at least about 100 mg/mL, or at least about 200 mg/mL, or at least about 500 mg/mL, or more than 500 mg/mL. In some embodiments, the present invention provides compositions (e.g., pharmaceutical compositions) that comprise a peptide of the invention in an aqueous solution at a concentration of less than 0.1 mg/mL, or about 0.1-0.5 mg/mL, or 0.5-1 mg/mL, or about 1-5 mg/mL, or about 5-10 mg/mL, or about 10-15 mg/mL, or about 15-20 mg/mL, or about 20-25 mg/mL, or about 25-30 mg/mL, or about 30-35 mg/mL, or about 35-40 mg/mL, or about 40-45 mg/mL, or about 45-50 mg/mL, or about 50-55 mg/mL, or about 55-60 mg/mL, or about 60-65 mg/mL, or about 65-70 mg/mL, or about 70-75 mg/mL, or about 75-80 mg/mL, or about 80-85 mg/mL, or about 85-90 mg/mL, or about 90-95 mg/mL, or about 95-100 mg/mL, or about 100-125 mg/mL, or about 125-150 mg/mL, or about 150-200 mg/mL, or about 200-250 mg/mL, or about 250-300 mg/mL, or about 300-350 mg/mL, or about 350-400 mg/mL, or about 400-500 mg/mL, or about 500-600 mg/mL or about 600-700 mg/mL, or about 700-1000 mg/mL, or more than 1000 mg/mL. In some embodiments, the present invention provides compositions (e.g., pharmaceutical compositions) that comprise a peptide of the invention in a non-aqueous solution at a concentration of about 0.5-1 mg/mL, or about 1-5 mg/mL, or about 5-10 mg/mL, or

about 10-15 mg/mL, or about 15-20 mg/mL, or about 20-25 mg/mL, or about 25-30 mg/mL, or about 30-35 mg/mL, or about 35-40 mg/mL, or about 40-45 mg/mL, or about 45-50 mg/mL, or about 50-55 mg/mL, or about 55-60 mg/mL, or about 60-65 mg/mL, or about 65-70 mg/mL, or about 70-75 mg/mL, or about 75-80 mg/mL, or about 80-85 mg/mL, or about 85-90 mg/mL, or
5 about 90-95 mg/mL, or about 95-100 mg/mL, or about 100-125 mg/mL, or about 125-150 mg/mL, or about 150-200 mg/mL, or about 200-250 mg/mL, or about 250-300 mg/mL, or about 300-350 mg/mL, or about 350-400 mg/mL, or about 400-500 mg/mL, or about 500-600 mg/mL or about 600-700 mg/mL, or about 700-1000 mg/mL, or more than 1000 mg/mL.

In some embodiments, the compositions (e.g., pharmaceutical compositions) may include
10 flavorings, odorants, or flavor or odor masking agents. In some embodiments, the flavorings may include non-acidic flavorings to prevent a decrease in solubility of the peptide. Such flavorings may include vanilla or maple syrup.

In some embodiments, pharmaceutical compositions according to the invention may contain 0.001%-95% of the peptides of the invention, preferably 1%-70%.

15 In some embodiments, the compositions (e.g., pharmaceutical compositions) of the present invention are provided in a dosage form. Such forms may be solutions, suspensions, emulsions, tablets, pills, suppositories, capsules, lozenges, wafers, powders (e.g. lyophilized powders), gels, creams, ointments, foams, pastes, patches, ampoules, vials, pre-filled syringes, sustained-release formulations, and the like.

20 In some embodiments, the compositions (e.g., pharmaceutical compositions) of the present invention are formulated for oral delivery, and may, for example, be provided in a solid dosage form such as a tablet, pill, capsule, lozenge, wafer, powder, or paste dosage form. In some embodiments, the compositions (e.g., pharmaceutical compositions) of the present invention are formulated for oral delivery, and may, for example, be provided in a liquid dosage form such as
25 an aqueous solution or suspension, or a non-aqueous solution or suspension. In some such embodiments the compositions may comprise one or more carriers such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, cellulose, magnesium carbonate, etc. In some such embodiments the compositions may comprise a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose; a disintegrating agent such as
30 alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate; or a glidant such as colloidal silicon dioxide. When the dosage form is a capsule, it can contain, in addition to materials of the above type, a liquid carrier such as fatty oil. In addition, dosage form can contain various other materials which modify the physical form of the dosage form, for example, coatings of sugar, shellac, or other enteric agents. The tablets of the invention can further be film

coated. Additional examples of suitable carriers are described in: Remington's Pharmaceutical Sciences" by E. W. Martin, the contents of which are hereby incorporated by reference herein.

In some embodiments, the compositions (e.g., pharmaceutical compositions) of the invention may be conveniently provided in unit dosage forms. Unit dosage forms are those containing a
5 single dose or unit (e.g., an effective amount), or an appropriate fraction thereof, of the peptides of the invention. The unit dosage forms may be presented in single-dose or multi-dose containers.

In some embodiments, the compositions (e.g., pharmaceutical compositions) of the invention may be provided in sealed ampoules or vials and may be stored in a freeze-dried (lyophilized)
10 condition requiring only the addition of a sterile liquid carrier (e.g., water) immediately prior to use.

In some embodiments, the compositions (e.g., pharmaceutical compositions) of the present invention may include agents or encapsulations that control the release of the peptide. In some
embodiments, the compositions (e.g., pharmaceutical compositions) of the present invention can
15 be co-administered with agents that prolong the activity or decrease the clearance of the peptides such as but not limited to co-administration with probenecid, ritonavir, CYP450 inhibitors (such as 1-Aminobenzotriazole).

7. Kits

To facilitate use of the invention, any of the peptides and/or compositions described herein can
20 be provided in the form of a kit. Such a kit will typically comprise one or more peptides and/or compositions described herein together with one or more of: a container, a delivery device, instructions for use (e.g., instructions regarding the timing and/or route of administration, instructions regarding dosing, etc.) packaging materials, and the like.

8. Methods of Use and Methods of Treatment

25 As described above and elsewhere herein, the peptides of the present invention have delta opioid receptor agonist activity.

Accordingly, in some embodiments, the present invention provides methods of activating delta opioid receptors in vitro or in vivo, such methods comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, with an effective amount of a peptide or composition
30 of the present invention. Similarly, in some embodiments, the present invention provides methods of treating subjects having a condition amenable to treatment with a delta opioid

receptor agonist (such as pain), such methods comprising administering an effective amount of a peptide or pharmaceutical composition of the present invention to such subjects.

In some embodiments, the present invention provides methods of treating pain in subjects in need thereof, such methods comprising administering an effective amount of a pharmaceutical composition of the present invention to the subject. Such methods may also be referred to herein as methods of inducing analgesia. The term “pain” as used herein refers to and encompasses all types of physical pain, and also encompasses pain of varying severity (e.g., mild, moderate and severe pain) and pain of different durations (e.g., acute pain and chronic pain).

In some embodiments, the methods of the present invention are used to treat mild pain. In some embodiments, the methods of the present invention are used to treat moderate pain. In some embodiments, the methods of the present invention are used to treat severe pain. In some embodiments, the methods of the present invention are used to treat acute pain. In some embodiments, the methods of the present invention are used to treat chronic pain.

In some embodiments, the methods of the present invention are used to treat traumatic pain. In some embodiments, the methods of the present invention are used to treat traumatic pain resulting from physical injury. In some embodiments, the methods of the present invention are used to treat traumatic pain resulting from surgery.

In some embodiments, the methods of the present invention are used to treat pain associated with a malignant or neoplastic disease. In some embodiments, the methods of the present invention are used to treat pain associated with cancer. In some embodiments, the methods of the present invention are used to treat pain associated with cancer treatment.

In some embodiments, the methods of the present invention are used to treat pain associated with degenerative diseases, such as osteoarthritis, osteoporosis, or degenerative disc disease.

In some embodiments, the methods of the present invention are used to treat pain associated with inflammation or pain associated with an inflammatory disease or condition. Such types of pain include inflammation resulting from an immune response following surgery, inflammation resulting from an immune response following an infection, inflammation resulting from an immune response following an allergic reaction, inflammatory nociceptive pain, inflammatory arthritic pain, rheumatoid arthritis pain, pain associated with inflammatory lung diseases (such as asthma, acute respiratory distress syndrome, or chronic obstructive pulmonary disease (COPD)), pain associated with inflammatory diseases of the gum (such as gingivitis or periodontitis), pain associated with inflammatory diseases of the kidney (e.g., glomerulonephritis), pain associated with inflammatory diseases of the skin (e.g., sclerodermatitis, psoriasis or eczema,) or pain

associated with inflammatory diseases of the central nervous system (such as chronic demyelinating diseases, multiple sclerosis, AIDS-related neurodegeneration, Alzheimer's disease, infectious meningitis, encephalomyelitis, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, viral encephalitis or autoimmune encephalitis).

5 In some embodiments, the methods of the present invention are used to treat pain associated with an autoimmune disease (such as psoriatic arthritis, rheumatoid arthritis (RA), Sjögren's syndrome, systemic lupus erythematosus (Lupus, SLE), Crohn's disease, Celiac disease, ulcerative colitis, Graves' disease, Hashimoto's thyroiditis, Addison's disease, dermatomyositis, psoriasis, Guillain-Barre syndrome, multiple sclerosis (MS), myasthenia gravis, autoimmune
10 vasculitis, type 1 diabetes, pernicious anemia, or vasculitis).

In some embodiments, the methods of the present invention are used to treat pain associated with an infectious disease. In some embodiments, the methods of the present invention are used to treat pain associated with a viral infection. In some embodiments, the methods of the present invention are used to treat pain associated with a bacterial infection. In some embodiments, the
15 methods of the present invention are used to treat pain associated with a parasitic infection. In some embodiments, the methods of the present invention are used to treat pain associated with a fungal infection. In some embodiments, the methods of the present invention are used to treat pain associated with tuberculosis, leprosy, or herpes. In some embodiments, the methods of the present invention are used to treat pain associated with a herpes infection, such as acute herpetic
20 pain or post herpetic pain. In some embodiments, the methods of the present invention are used to treat pain associated with HIV infection or AIDS.

In some embodiments, the methods of the present invention are used to treat pain associated with Type I or Type II diabetes mellitus (such as pain associated with diabetic cataracts, glaucoma, retinopathy, nephropathy, microalbuminuria, progressive diabetic nephropathy, polyneuropathy,
25 mononeuropathies, autonomic neuropathy, gangrene of the feet, foot ulcers, atherosclerotic coronary arterial disease, peripheral arterial disease or diabetic joint problems).

In some embodiments, the methods of the present invention are used to treat neuropathic pain, such as pain associated with sciatica, diabetic neuropathy, causalgia, brachial plexus avulsion, occipital neuralgia, trigeminal neuralgia, fibromyalgia, vulvodynia, allodynia, prostatic pain, gout,
30 phantom limb pain, and other forms of neuralgia such as neuralgia associated with other neuropathic pain syndromes or complex regional pain syndrome.

In some embodiments, the methods of the present invention are used to treat idiopathic pain syndromes.

In some embodiments, the methods of the present invention are used to treat localized or tissue-specific pain, such as headache (including migraine headache, tension headache, cluster headache), ocular pain (e.g. glaucoma pain) corneal pain, bone pain, joint pain, back pain (e.g. back pain associated with a herniated disc, spinal stenosis, spinal root lesion, or spinal root
5 impingement), neck pain, muscle pain, tendon pain, fibrous tissue pain, ligament pain, pelvic pain urogenital pain, interstitial cystitis pain, uterine pain, pain from uterine fibroids, menstrual pain, gastrointestinal pain (e.g., pain associated with irritable bowel syndrome (IBS), irritable bowel disease (IBD), Crohn's disease, Gastroesophageal reflux disease (GERD)), heart pain, skin pain, burn pain, lung pain, visceral pain (e.g., kidney pain, liver pain, spleen pain, gall
10 bladder pain, etc.), bone pain, or dental pain.

It should be noted that the categorization of pain types provided above are not mutually exclusive. For example, some types of localized or tissue-specific pain are also inflammatory pain, some types of neuropathic pain are also tissue-specific pain or inflammatory pain, and the like. The categorization of pain types listed above is provided for convenience and is not
15 intended to be limiting or exclusive.

Subjects that can be treated using the methods of the present invention include any mammalian subjects that express a delta opioid receptor to which the peptides of the invention bind and have agonist activity. In some embodiments, the subjects are non-human mammals useful for conducting preclinical studies, such as a rodent (e.g., mice or rats) or non-human primates. In
20 some embodiments, the subjects are humans.

The treatment methods provided herein involve administering the peptides or pharmaceutical compositions of the present invention to subjects. Various routes and systems for administration are known in the art and any such suitable route or system can be used to administer the peptides and pharmaceutical compositions of the present invention to subjects. In some embodiments,
25 parenteral administration is used. In some embodiments, enteral administration is used. Contemplated parenteral or enteral administration routes include, but are not limited to, intradermal, intramuscular (IM), intraperitoneal (IP), intravenous (IV) (e.g., as a bolus injection or by infusion), subcutaneous, intranasal, epidural, intracerebral, intrathecal, topical, transepithelial (e.g., by absorption through oral, rectal, gastric, esophageal, or intestinal mucosa,
30 etc.), sublingual, and oral (PO) administration routes. In some embodiments, administration is systemic. In some embodiments, administration is local. In some embodiments, administration is intravenous (IV), subcutaneous (SC), or oral (PO). In some embodiments, administration is oral (PO).

In some embodiments, an “effective amount” of the peptides or compositions of the present invention is administered to subjects. The “effective amount” in a given situation may depend on variety of factors including, but not limited to, the species of the subject (e.g., whether a human or some other animal species), the age of the subject, the sex of the subject, the weight of the subject, the formulation of the peptide, the route of administration, the planned dosing regimen, etc. The effective amount (which may be a range of effective amounts) can be determined by standard techniques, for example using in vitro assays and/or in vivo assays in the intended subject species or any suitable animal model species. Suitable methods for determining an effective amount include, but are not limited to, dose-escalation studies, extrapolation from dose-response curves, and/or extrapolation from other data derived from in vitro and/or in vivo model systems. In some embodiments, the effective amount may be determined according to the judgment of a medical or veterinary practitioner based on the specific circumstances.

The peptides and/or compositions described herein may be administered to subjects according to any suitable administration regimen or dosing schedule. In some embodiments, a single dose is administered. In some embodiments, multiple doses are administered. In some embodiments a suitable administration regimen may comprise administration of 1, or 2, or 3, or more doses per day. In some embodiments, a suitable administration regimen may comprise administration of 1, 2, 3, 4, 5, 6, 7, or more doses per week. In some embodiments, a suitable administration regimen may comprise administration of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more doses per month.

In some embodiments, the peptides of the present invention are administered to human subjects at a dose of from about 1 mg/kg to 1000 mg/kg. In some embodiments, the peptides of the present invention are administered to human subjects at a dose of from about 50 mg to 50 g.

In some embodiments, the peptides of the present invention are administered to human subjects orally at any of the doses described above.

In some embodiments, the peptides of the present invention are administered to human subjects orally about every 3 hours, about every 4 hours, about every 5 hours, about every 6 hours, about every 7 hours, about every 8 hours, about every 9 hours, about every 10 hours, about every 11 hours, about every 12 hours, about every 13 hours, about every 14 hours, about every 15 hours, about every 16 hours, about every 17 hours, about every 18 hours, about every 19 hours, about every 20 hours, about every 21 hours, about every 22 hours, about every 23 hours, or about every 24 hours. In some embodiments, the peptides of the present invention are administered to human subjects orally as needed to control pain.

- In some embodiments, administration of the peptides or compositions of the present invention can be performed in conjunction with administration of one or more additional active agents. Examples of such additional active agents include, but are not limited to agents: (a) that increase an effect produced by a delta opioid agonist peptide of the present invention, (b) that reduce an undesirable side effect of a delta opioid agonist peptide of the present invention, (c) that increase a desirable side effect produced by a delta opioid agonist peptide of the present invention, (d) that are useful in the treatment of acute or chronic pain (including but not limited to mu opioid agonists or partial agonists, kappa opioid agonists, acetaminophen, ibuprofen, aspirin, naproxen, gabapentinoids, ketamine, local anesthetics, skeletal muscle relaxants, sodium channel inhibitors, serotonin norepinephrine reuptake inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, CGRP inhibitors, and/or DOR agonists or partial agonists), or (e) that are useful in the treatment or prevention of addiction or substance abuse (including but not limited to: mu opioid agonists or partial agonists, mu opioid antagonists, selective serotonin reuptake inhibitors, bupropion, and/or DOR agonists or partial agonists).
- In further embodiments the present invention also provides methods of treatment that comprise administering to a subject in need thereof an effective amount of a cell or vector or nucleic acid sequence capable of causing the expression and/or production of one or more of the peptides of the present invention within the subject.

- Those of skill in the art will appreciate that, in addition to being useful in methods of treatment, the peptides of the invention may be useful for a variety of other applications. For example, the peptides of the invention may be useful as research tools (e.g., for studying the effects of delta opioid receptor activation in vitro or in vivo), and/or as diagnostic tools (e.g., for detecting, assaying, and/or quantifying delta opioid receptors). All such uses are within the scope of the present invention.

9. Additional Embodiments

- The present invention provides additional embodiments that are enumerated below in this section. These additional embodiments are numbered with an associated additional embodiment number ("AE NO"). One of ordinary skill in the art will appreciate that each of these embodiments can be combined in various different ways. All such combinations are contemplated and fall within the scope of the present invention.

1. An isolated peptide consisting of the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 1-304.

2. A peptide comprising the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 1-304.
3. A peptide according to AE NO 1, wherein the peptide is in the form of a sodium salt.
4. A pharmaceutical composition comprising a peptide according to AE NO 1 and at least
5 one pharmaceutically acceptable carrier or excipient.
5. A pharmaceutical composition comprising the peptide of AE NO 3, and at least one pharmaceutically acceptable carrier or excipient.
6. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a
10 peptide according to AE NO 1 or AE NO 3 or a pharmaceutical composition according to AE NO 4 or AE NO 5.
7. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering a therapeutically effective amount of a peptide according to AE NO 1 or AE NO 3 or a pharmaceutical composition
15 according to AE NO 4 or AE NO 5, to the subject.
8. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 1 or AE NO 3 or a pharmaceutical composition according to AE NO 4 or AE NO 5, the method comprising administering an effective amount of a peptide according to AE NO 1 or AE NO 3 or a pharmaceutical composition according to
20 AE NO 4 or AE NO 5, to the subject.
9. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 1 or AE NO 3 or a pharmaceutical composition according to AE NO 4 or AE NO 5, to the subject.
- 25 10. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 1 or AE NO 3 or a pharmaceutical composition according to AE NO 4 or AE NO 5, to the subject.
11. The method of AE NO 7, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
- 30 12. The method of AE NO 11, wherein the condition is pain.
13. An isolated nucleic acid molecule that encodes the peptide of AE NO 1.
14. An expression vector comprising the nucleic acid molecule of AE NO 13.
15. A host cell comprising a nucleic acid molecule according to AE NO 13 or an expression vector according to AE NO 14.

16. An isolated peptide consisting of the amino acid sequence {n-acet-D}SYGEVGVRQAPFPSRAS{c-amid-C}(PEP NO: and/or SEQ ID NO: 16).
17. A peptide comprising the amino acid sequence {n-acet-D}SYGEVGVRQAPFPSRAS{c-amid-C}(PEP NO: and/or SEQ ID NO: 16).
- 5 18. A peptide according to AE NO 16, wherein the peptide is in the form of a sodium salt.
19. A pharmaceutical composition comprising a peptide according to AE NO 16 and at least one pharmaceutically acceptable carrier or excipient.
20. A pharmaceutical composition comprising the peptide of AE NO 18, and at least one pharmaceutically acceptable carrier or excipient.
- 10 21. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 16 or AE NO 18 or a pharmaceutical composition according to AE NO 19 or AE NO 20.
22. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 16 or AE NO 18 or a pharmaceutical composition according to AE NO 19 or AE NO 20, to the subject.
- 15 23. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 16 or AE NO 18 or a pharmaceutical composition according to AE NO 19 or AE NO 20, the method comprising administering an effective amount of a peptide according to AE NO 16 or AE NO 18 or a pharmaceutical composition according to AE NO 19 or AE NO 20, to the subject.
- 20 24. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 16 or AE NO 18 or a pharmaceutical composition according to AE NO 19 or AE NO 20, to the subject.
- 25 25. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 16 or AE NO 18 or a pharmaceutical composition according to AE NO 19 or AE NO 20, to the subject.
- 30 26. The method of AE NO 22, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
27. The method of AE NO 26, wherein the condition is pain.
28. An isolated nucleic acid molecule that encodes the peptide of AE NO 16.
29. An expression vector comprising the nucleic acid molecule of AE NO 28

30. A host cell comprising a nucleic acid molecule according to AE NO 28 or an expression vector according to AE NO 29.
31. An isolated peptide consisting of the amino acid sequence {n-acet-
{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}} (PEP NO:
5 and/or SEQ ID NO: 17).
32. A peptide comprising the amino acid sequence {n-acet-
{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{dR}{dA}{dS}{c-amid-{dC}} (PEP NO:
and/or SEQ ID NO: 17).
33. A peptide according to AE NO 31, wherein the peptide is in the form of a sodium salt.
- 10 34. A pharmaceutical composition comprising a peptide according to AE NO 31 and at least one pharmaceutically acceptable carrier or excipient.
35. A pharmaceutical composition comprising the peptide of AE NO 33, and at least one pharmaceutically acceptable carrier or excipient.
- 15 36. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 31 or AE NO 33 or a pharmaceutical composition according to AE NO 34 or AE NO 35.
37. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a
20 peptide according to AE NO 31 or AE NO 33 or a pharmaceutical composition according to AE NO 34 or AE NO 35, to the subject.
38. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 31 or AE NO 33 or a pharmaceutical composition
25 according to AE NO 34 or AE NO 35, the method comprising administering an effective amount of a peptide according to AE NO 31 or AE NO 33 or a pharmaceutical composition according to AE NO 34 or AE NO 35, to the subject.
39. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 31 or AE NO 33 or a pharmaceutical composition according to AE
30 NO 34 or AE NO 35, to the subject.
40. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 31 or AE NO 33 or a pharmaceutical composition according to AE NO 34 or AE NO 35, to the subject.
41. The method of AE NO 37, wherein the condition is pain, depression, anxiety, addiction,
35 or substance abuse.

42. The method of AE NO 41, wherein the condition is pain.
43. An isolated nucleic acid molecule that encodes the peptide of AE NO 31.
44. An expression vector comprising the nucleic acid molecule of AE NO 43.
45. A host cell comprising a nucleic acid molecule according to AE NO 43 or an expression
5 vector according to AE NO 44.
46. An isolated peptide consisting of the amino acid sequence {n-acet-
{dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{dS}{c-amid-{dC}} (PEP
NO: and/or SEQ ID NO: 24).
47. A peptide comprising the amino acid sequence {n-acet-
10 {dβD}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{dS}{c-amid-{dC}} (PEP
NO: and/or SEQ ID NO: 24).
48. A peptide according to AE NO 46, wherein the peptide is in the form of a sodium salt.
49. A pharmaceutical composition comprising a peptide according to AE NO 46 and at least
one pharmaceutically acceptable carrier or excipient.
- 15 50. A pharmaceutical composition comprising the peptide of AE NO 48, and at least one
pharmaceutically acceptable carrier or excipient.
51. A method of activating a delta opioid receptor, the method comprising contacting a delta
opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a
peptide according to AE NO 46 or AE NO 48 or a pharmaceutical composition according
20 to AE NO 49 or AE NO 50.
52. A method of treating a mammalian subject having a condition amenable to treatment with
a delta opioid receptor, the method comprising administering an effective amount of a
peptide according to AE NO 46 or AE NO 48 or a pharmaceutical composition according
to AE NO 49 or AE NO 50, to the subject.
- 25 53. A method of treating a mammalian subject having a condition amenable to treatment with
a peptide according to AE NO 46 or AE NO 48 or a pharmaceutical composition
according to AE NO 49 or AE NO 50, the method comprising administering an effective
amount of a peptide according to AE NO 46 or AE NO 48 or a pharmaceutical
composition according to AE NO 49 or AE NO 50, to the subject.
- 30 54. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject
in need thereof, the method comprising administering an effective amount of a peptide
according to AE NO 46 or AE NO 48 or a pharmaceutical composition according to AE
NO 49 or AE NO 50, to the subject.

55. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 46 or AE NO 48 or a pharmaceutical composition according to AE NO 49 or AE NO 50, to the subject.
56. The method of AE NO 53, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
57. The method of AE NO 56, wherein the condition is pain.
58. An isolated nucleic acid molecule that encodes the peptide of AE NO 46.
59. An expression vector comprising the nucleic acid molecule of AE NO 58.
60. A host cell comprising a nucleic acid molecule according to AE NO 58 or an expression vector according to AE NO 59.
61. An isolated peptide consisting of the amino acid sequence {n-acet-{d β D}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{c-amid-{dS}} (PEP NO: and/or SEQ ID NO: 157).
62. A peptide comprising the amino acid sequence {n-acet-{d β D}}{dS}{dY}GEVGVRQAPF{dP}{dS}{r-pal-K}{dA}{c-amid-{dS}} (PEP NO: and/or SEQ ID NO: 157).
63. A peptide according to AE NO 61, wherein the peptide is in the form of a sodium salt.
64. A pharmaceutical composition comprising a peptide according to AE NO 61 and at least one pharmaceutically acceptable carrier or excipient.
65. A pharmaceutical composition comprising the peptide of AE NO 63, and at least one pharmaceutically acceptable carrier or excipient.
66. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 61 or AE NO 63 or a pharmaceutical composition according to AE NO 64 or AE NO 65.
67. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 61 or AE NO 63 or a pharmaceutical composition according to AE NO 64 or AE NO 65, to the subject.
68. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 61 or AE NO 63 or a pharmaceutical composition according to AE NO 64 or AE NO 65, the method comprising administering an effective amount of a peptide according to AE NO 61 or AE NO 63 or a pharmaceutical composition according to AE NO 64 or AE NO 65, to the subject.

69. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 61 or AE NO 63 or a pharmaceutical composition according to AE NO 64 or AE NO 65, to the subject.
- 5 70. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 61 or AE NO 63 or a pharmaceutical composition according to AE NO 64 or AE NO 65, to the subject.
71. The method of AE NO 67, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
- 10 72. The method of AE NO 71, wherein the condition is pain.
73. An isolated nucleic acid molecule that encodes the peptide of AE NO 61.
74. An expression vector comprising the nucleic acid molecule of AE NO 73.
75. A host cell comprising a nucleic acid molecule according to AE NO 73 or an expression vector according to AE NO 74.
- 15 76. An isolated peptide consisting of the amino acid sequence {n-acet-D}SYGEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 162).
77. A peptide comprising the amino acid sequence {n-acet-D}SYGEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 162).
78. A peptide according to AE NO 76, wherein the peptide is in the form of a sodium salt.
- 20 79. A pharmaceutical composition comprising a peptide according to AE NO 76 and at least one pharmaceutically acceptable carrier or excipient.
80. A pharmaceutical composition comprising the peptide of AE NO 78, and at least one pharmaceutically acceptable carrier or excipient.
81. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 76 or AE NO 78 or a pharmaceutical composition according to AE NO 79 or AE NO 80.
- 25 82. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 76 or AE NO 78 or a pharmaceutical composition according to AE NO 79 or AE NO 80, to the subject.
- 30 83. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 76 or AE NO 78 or a pharmaceutical composition according to AE NO 79 or AE NO 80, the method comprising administering an effective

- amount of a peptide according to AE NO 76 or AE NO 78 or a pharmaceutical composition according to AE NO 79 or AE NO 80, to the subject.
84. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 76 or AE NO 78 or a pharmaceutical composition according to AE NO 79 or AE NO 80, to the subject.
85. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 76 or AE NO 78 or a pharmaceutical composition according to AE NO 79 or AE NO 80, to the subject.
86. The method of AE NO 82, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
87. The method of AE NO 86, wherein the condition is pain.
88. An isolated nucleic acid molecule that encodes the peptide of AE NO 76.
89. An expression vector comprising the nucleic acid molecule of AE NO 88.
90. A host cell comprising a nucleic acid molecule according to AE NO 88 or an expression vector according to AE NO 89.
91. An isolated peptide consisting of the amino acid sequence {n-acet-Y}GEVGVRQAPF{c-amid-P} (PEP NO: and/or SEQ ID NO: 163).
92. A peptide comprising the amino acid sequence {n-acet-Y}GEVGVRQAPF{c-amid-P} (PEP NO: and/or SEQ ID NO: 163).
93. A peptide according to AE NO 91, wherein the peptide is in the form of a sodium salt.
94. A pharmaceutical composition comprising a peptide according to AE NO 91 and at least one pharmaceutically acceptable carrier or excipient.
95. A pharmaceutical composition comprising the peptide of AE NO 93, and at least one pharmaceutically acceptable carrier or excipient.
96. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 91 or AE NO 93 or a pharmaceutical composition according to AE NO 94 or AE NO 95.
97. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 91 or AE NO 93 or a pharmaceutical composition according to AE NO 94 or AE NO 95, to the subject.
98. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 91 or AE NO 93 or a pharmaceutical composition

- according to AE NO 94 or AE NO 95, the method comprising administering an effective amount of a peptide according to AE NO 91 or AE NO 93 or a pharmaceutical composition according to AE NO 94 or AE NO 95, to the subject.
99. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject
5 in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 91 or AE NO 93 or a pharmaceutical composition according to AE NO 94 or AE NO 95, to the subject.
100. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 91 or AE NO 93 or a
10 pharmaceutical composition according to AE NO 94 or AE NO 95, to the subject.
101. The method of AE NO 97, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
102. The method of AE NO 101, wherein the condition is pain.
103. An isolated nucleic acid molecule that encodes the peptide of AE NO 91.
- 15 104. An expression vector comprising the nucleic acid molecule of AE NO 103.
105. A host cell comprising a nucleic acid molecule according to AE NO 103 or an expression vector according to AE NO 104.
106. An isolated peptide consisting of the amino acid sequence {n-acet-Y}GEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 164).
- 20 107. A peptide comprising the amino acid sequence {n-acet-Y}GEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 164).
108. A peptide according to AE NO 106, wherein the peptide is in the form of a sodium salt.
109. A pharmaceutical composition comprising a peptide according to AE NO 106 and at least one pharmaceutically acceptable carrier or excipient.
- 25 110. A pharmaceutical composition comprising the peptide of AE NO 108, and at least one pharmaceutically acceptable carrier or excipient.
111. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 106 or AE NO 108 or a pharmaceutical composition
30 according to AE NO 109 or AE NO 110.
112. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 106 or AE NO 108 or a pharmaceutical composition according to AE NO 109 or AE NO 110, to the subject.

113. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 106 or AE NO 108 or a pharmaceutical composition according to AE NO 109 or AE NO 110, the method comprising administering an effective amount of a peptide according to AE NO 106 or AE NO 108 or a pharmaceutical composition according to AE NO 109 or AE NO 110, to the subject.
114. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 106 or AE NO 108 or a pharmaceutical composition according to AE NO 109 or AE NO 110, to the subject.
115. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 106 or AE NO 108 or a pharmaceutical composition according to AE NO 109 or AE NO 110, to the subject.
116. The method of AE NO 112, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
117. The method of AE NO 116, wherein the condition is pain.
118. An isolated nucleic acid molecule that encodes the peptide of AE NO 106.
119. An expression vector comprising the nucleic acid molecule of AE NO 118.
120. A host cell comprising a nucleic acid molecule according to AE NO 118 or an expression vector according to AE NO 119.
121. An isolated peptide consisting of the amino acid sequence {n-acet-D}SYGEVGVRQAPF{c-amid-P} (PEP NO: and/or SEQ ID NO: 165).
122. A peptide comprising the amino acid sequence {n-acet-D}SYGEVGVRQAPF{c-amid-P} (PEP NO: and/or SEQ ID NO: 165).
123. A peptide according to AE NO 121, wherein the peptide is in the form of a sodium salt.
124. A pharmaceutical composition comprising a peptide according to AE NO 121 and at least one pharmaceutically acceptable carrier or excipient.
125. A pharmaceutical composition comprising the peptide of AE NO 123, and at least one pharmaceutically acceptable carrier or excipient.
126. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 121 or AE NO 123 or a pharmaceutical composition according to AE NO 124 or AE NO 125.
127. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a

- peptide according to AE NO 121 or AE NO 123 or a pharmaceutical composition according to AE NO 124 or AE NO 125, to the subject.
128. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 121 or AE NO 123 or a pharmaceutical composition according to AE NO 124 or AE NO 125, the method comprising administering an effective amount of a peptide according to AE NO 121 or AE NO 123 or a pharmaceutical composition according to AE NO 124 or AE NO 125, to the subject.
129. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 121 or AE NO 123 or a pharmaceutical composition according to AE NO 124 or AE NO 125, to the subject.
130. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 121 or AE NO 123 or a pharmaceutical composition according to AE NO 124 or AE NO 125, to the subject.
131. The method of AE NO 127, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
132. The method of AE NO 131, wherein the condition is pain.
133. An isolated nucleic acid molecule that encodes the peptide of AE NO 121.
134. An expression vector comprising the nucleic acid molecule of AE NO 133.
135. A host cell comprising a nucleic acid molecule according to AE NO 133 or an expression vector according to AE NO 134.
136. An isolated peptide consisting of the amino acid sequence {n-acet-Y}GEVGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 167).
137. A peptide comprising the amino acid sequence {n-acet-Y}GEVGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 167).
138. A peptide according to AE NO 136, wherein the peptide is in the form of a sodium salt.
139. A pharmaceutical composition comprising a peptide according to AE NO 136 and at least one pharmaceutically acceptable carrier or excipient.
140. A pharmaceutical composition comprising the peptide of AE NO 138, and at least one pharmaceutically acceptable carrier or excipient.
141. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 136 or AE NO 138 or a pharmaceutical composition according to AE NO 139 or AE NO 140.

142. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 136 or AE NO 138 or a pharmaceutical composition according to AE NO 139 or AE NO 140, to the subject.
- 5 143. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 136 or AE NO 138 or a pharmaceutical composition according to AE NO 139 or AE NO 140, the method comprising administering an effective amount of a peptide according to AE NO 136 or AE NO 138 or a pharmaceutical composition according to AE NO 139 or AE NO 140, to the subject.
- 10 144. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 136 or AE NO 138 or a pharmaceutical composition according to AE NO 139 or AE NO 140, to the subject.
- 15 145. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 136 or AE NO 138 or a pharmaceutical composition according to AE NO 139 or AE NO 140, to the subject.
146. The method of AE NO 142, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
147. The method of AE NO 146, wherein the condition is pain.
- 20 148. An isolated nucleic acid molecule that encodes the peptide of AE NO 136.
149. An expression vector comprising the nucleic acid molecule of AE NO 148.
150. A host cell comprising a nucleic acid molecule according to AE NO 148 or an expression vector according to AE NO 149.
- 25 151. An isolated peptide consisting of the amino acid sequence {n-pal-V}GVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 171).
152. A peptide comprising the amino acid sequence {n-pal-V}GVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 171).
153. A peptide according to AE NO 151, wherein the peptide is in the form of a sodium salt.
154. A pharmaceutical composition comprising a peptide according to AE NO 151 and at least one pharmaceutically acceptable carrier or excipient.
- 30 155. A pharmaceutical composition comprising the peptide of AE NO 153, and at least one pharmaceutically acceptable carrier or excipient.
156. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a

- peptide according to AE NO 151 or AE NO 153 or a pharmaceutical composition according to AE NO 154 or AE NO 155.
157. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 151 or AE NO 153 or a pharmaceutical composition according to AE NO 154 or AE NO 155, to the subject.
158. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 151 or AE NO 153 or a pharmaceutical composition according to AE NO 154 or AE NO 155, the method comprising administering an effective amount of a peptide according to AE NO 151 or AE NO 153 or a pharmaceutical composition according to AE NO 154 or AE NO 155, to the subject.
159. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 151 or AE NO 153 or a pharmaceutical composition according to AE NO 154 or AE NO 155, to the subject.
160. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 151 or AE NO 153 or a pharmaceutical composition according to AE NO 154 or AE NO 155, to the subject.
161. The method of AE NO 157, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
162. The method of AE NO 161, wherein the condition is pain.
163. An isolated nucleic acid molecule that encodes the peptide of AE NO 151.
164. An expression vector comprising the nucleic acid molecule of AE NO 163.
165. A host cell comprising a nucleic acid molecule according to AE NO 163 or an expression vector according to AE NO 164.
166. An isolated peptide consisting of the amino acid sequence {n-pal-Y}GEVGV{hR}QA{c-amid-P} (PEP NO: and/or SEQ ID NO: 175).
167. A peptide comprising the amino acid sequence {n-pal-Y}GEVGV{hR}QA{c-amid-P} (PEP NO: and/or SEQ ID NO: 175).
168. A peptide according to AE NO 166, wherein the peptide is in the form of a sodium salt.
169. A pharmaceutical composition comprising a peptide according to AE NO 166 and at least one pharmaceutically acceptable carrier or excipient.
170. A pharmaceutical composition comprising the peptide of AE NO 168, and at least one pharmaceutically acceptable carrier or excipient.

171. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 166 or AE NO 168 or a pharmaceutical composition according to AE NO 169 or AE NO 170.
- 5 172. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 166 or AE NO 168 or a pharmaceutical composition according to AE NO 169 or AE NO 170, to the subject.
- 10 173. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 166 or AE NO 168 or a pharmaceutical composition according to AE NO 169 or AE NO 170, the method comprising administering an effective amount of a peptide according to AE NO 166 or AE NO 168 or a pharmaceutical composition according to AE NO 169 or AE NO 170, to the subject.
- 15 174. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 166 or AE NO 168 or a pharmaceutical composition according to AE NO 169 or AE NO 170, to the subject.
- 20 175. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 166 or AE NO 168 or a pharmaceutical composition according to AE NO 169 or AE NO 170, to the subject.
176. The method of AE NO 172, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
177. The method of AE NO 176, wherein the condition is pain.
178. An isolated nucleic acid molecule that encodes the peptide of AE NO 166.
- 25 179. An expression vector comprising the nucleic acid molecule of AE NO 178.
180. A host cell comprising a nucleic acid molecule according to AE NO 178 or an expression vector according to AE NO 179.
181. An isolated peptide consisting of the amino acid sequence {n-pal-G}LMGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 182).
- 30 182. A peptide comprising the amino acid sequence {n-pal-G}LMGVRQA{c-amid-P} (PEP NO: and/or SEQ ID NO: 182).
183. A peptide according to AE NO 181, wherein the peptide is in the form of a sodium salt.
184. A pharmaceutical composition comprising a peptide according to AE NO 181 and at least one pharmaceutically acceptable carrier or excipient.

185. A pharmaceutical composition comprising the peptide of AE NO 183, and at least one pharmaceutically acceptable carrier or excipient.
186. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 181 or AE NO 183 or a pharmaceutical composition according to AE NO 184 or AE NO 185.
187. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 181 or AE NO 183 or a pharmaceutical composition according to AE NO 184 or AE NO 185, to the subject.
188. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 181 or AE NO 183 or a pharmaceutical composition according to AE NO 184 or AE NO 185, the method comprising administering an effective amount of a peptide according to AE NO 181 or AE NO 183 or a pharmaceutical composition according to AE NO 184 or AE NO 185, to the subject.
189. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 181 or AE NO 183 or a pharmaceutical composition according to AE NO 184 or AE NO 185, to the subject.
190. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 181 or AE NO 183 or a pharmaceutical composition according to AE NO 184 or AE NO 185, to the subject.
191. The method of AE NO 187, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
192. The method of AE NO 191, wherein the condition is pain.
193. An isolated nucleic acid molecule that encodes the peptide of AE NO 181.
194. An expression vector comprising the nucleic acid molecule of AE NO 193.
195. A host cell comprising a nucleic acid molecule according to AE NO 193 or an expression vector according to AE NO 194.
196. An isolated peptide consisting of the amino acid sequence {n-pal-D}SYGEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 186).
197. A peptide comprising the amino acid sequence {n-pal-D}SYGEVGVRQAPFPSRA{c-amid-S} (PEP NO: and/or SEQ ID NO: 186).
198. A peptide according to AE NO 196, wherein the peptide is in the form of a sodium salt.

199. A pharmaceutical composition comprising a peptide according to AE NO 196 and at least one pharmaceutically acceptable carrier or excipient.
200. A pharmaceutical composition comprising the peptide of AE NO 198, and at least one pharmaceutically acceptable carrier or excipient.
- 5 201. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 196 or AE NO 198 or a pharmaceutical composition according to AE NO 199 or AE NO 200.
202. A method of treating a mammalian subject having a condition amenable to treatment with
10 a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 196 or AE NO 198 or a pharmaceutical composition according to AE NO 199 or AE NO 200, to the subject.
203. A method of treating a mammalian subject having a condition amenable to treatment with
15 a peptide according to AE NO 196 or AE NO 198 or a pharmaceutical composition according to AE NO 199 or AE NO 200, the method comprising administering an effective amount of a peptide according to AE NO 196 or AE NO 198 or a pharmaceutical composition according to AE NO 199 or AE NO 200, to the subject.
204. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject
20 in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 196 or AE NO 198 or a pharmaceutical composition according to AE NO 199 or AE NO 200, to the subject.
205. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 196 or AE NO 198 or a pharmaceutical composition according to AE NO 199 or AE NO 200, to the subject.
- 25 206. The method of AE NO 202, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
207. The method of AE NO 206, wherein the condition is pain.
208. An isolated nucleic acid molecule that encodes the peptide of AE NO 196.
209. An expression vector comprising the nucleic acid molecule of AE NO 208.
- 30 210. A host cell comprising a nucleic acid molecule according to AE NO 208 or an expression vector according to AE NO 209.
211. An isolated peptide consisting of the amino acid sequence {n-acet-D}SYGEVGVRQAPFPS{r-pal-K}A{c-amid-S} (PEP NO: and/or SEQ ID NO: 187).
212. A peptide comprising the amino acid sequence {n-acet-D}SYGEVGVRQAPFPS{r-pal-K}A{c-amid-S} (PEP NO: and/or SEQ ID NO: 187).
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213. A peptide according to AE NO 211, wherein the peptide is in the form of a sodium salt.
214. A pharmaceutical composition comprising a peptide according to AE NO 211 and at least one pharmaceutically acceptable carrier or excipient.
- 5 215. A pharmaceutical composition comprising the peptide of AE NO 213, and at least one pharmaceutically acceptable carrier or excipient.
216. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to AE NO 211 or AE NO 213 or a pharmaceutical composition according to AE NO 214 or AE NO 215.
- 10 217. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide according to AE NO 211 or AE NO 213 or a pharmaceutical composition according to AE NO 214 or AE NO 215, to the subject.
- 15 218. A method of treating a mammalian subject having a condition amenable to treatment with a peptide according to AE NO 211 or AE NO 213 or a pharmaceutical composition according to AE NO 214 or AE NO 215, the method comprising administering an effective amount of a peptide according to AE NO 211 or AE NO 213 or a pharmaceutical composition according to AE NO 214 or AE NO 215, to the subject.
- 20 219. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 211 or AE NO 213 or a pharmaceutical composition according to AE NO 214 or AE NO 215, to the subject.
220. A method of treating pain in a subject in need thereof, the method comprising administering an effective amount of a peptide according to AE NO 211 or AE NO 213 or a pharmaceutical composition according to AE NO 214 or AE NO 215, to the subject.
- 25 221. The method of AE NO 217, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
222. The method of AE NO 221, wherein the condition is pain.
223. An isolated nucleic acid molecule that encodes the peptide of AE NO 211.
- 30 224. An expression vector comprising the nucleic acid molecule of AE NO 223.
225. A host cell comprising a nucleic acid molecule according to AE NO 223 or an expression vector according to AE NO 224.
226. An isolated peptide comprising the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 1-304.

227. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 16, 17, 24, 86, 157, 162, 163, 164, 165, 166, 167, 170, 171, 173, 175, 177, 178, 179, 182, 183, 185, 186, or 187.
228. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 16.
229. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 17.
230. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 24.
231. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 86.
232. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 157.
233. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 162.
234. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 163.
235. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 164.
236. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 165.
237. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 166.
238. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 167.
239. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 170.
240. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 171.
241. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 173.
242. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 175.
243. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 177.

244. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 178.
245. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 179.
- 5 246. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 182.
247. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 183.
248. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 185.
- 10 249. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 186.
250. An isolated peptide according to AE NO 226, wherein the peptide comprises the amino acid sequence of PEP NO: and/or SEQ ID NO: 187.
- 15 251. An isolated peptide comprising an amino acid sequence that has at least 70% identity to any of PEP NOs: and/or SEQ ID NOs: 1-304, wherein the peptide is a delta opioid agonist.
252. An isolated peptide comprising an amino acid sequence that has at least 80% sequence identity to any of PEP NOs: and/or SEQ ID NOs: 1-304, wherein the peptide is a delta opioid agonist.
- 20 253. An isolated peptide comprising an amino acid sequence that has at least 90% sequence identity to the peptides of any of PEP NOs: and/or SEQ ID NOs: 1-304, wherein the peptide is a delta opioid agonist.
254. An isolated peptide comprising an amino acid sequence that has at least 95% sequence identity to the peptides of any of PEP NOs: and/or SEQ ID NOs: 1-304, wherein the peptide is a delta opioid agonist.
- 25 255. An isolated peptide according to any one of AE NOs 251-254, comprising one or more of the substitutions or deletions specified in Tables 2A-I.
256. An isolated peptide comprising an amino acid sequence that is a variant of the amino acid sequence of any of PEP NOs: and/or SEQ ID NOs: 1-304 having up to 5 amino acid residues substituted, added or deleted, wherein the peptide is a delta opioid agonist.
- 30 257. An isolated peptide according to AE NO 256, wherein the peptide has up to 4 amino acid residues substituted, added or deleted.
258. An isolated peptide according to AE NO 256, wherein the peptide has up to 3 amino acid residues substituted, added or deleted.
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259. An isolated peptide according to AE NO 256, wherein the peptide has up to 2 amino acid residues substituted, added or deleted.
260. An isolated peptide according to AE NO 256, wherein the peptide has up to 1 amino acid residues substituted, added or deleted.
- 5 261. An isolated peptide according to any one of AE NOs 256-260, wherein the substitutions, additions, or deletions are selected from those specified in Tables 2A-I.
262. An isolated peptide according to any of AE NOs 226-261, further comprising additional N-terminal and/or C-terminal amino acids.
263. An isolated peptide according to any of AE NOs 226-261, further comprising up to 5
10 additional N-terminal or C-terminal amino acids.
264. An isolated peptide according to any of AE NOs 226-261, wherein the peptide is a linear peptide.
265. An isolated peptide according to any of AE NOs 226-261, wherein the peptide is a non-linear peptide.
- 15 266. An isolated peptide according to AE NO 265, wherein the peptide is a branched peptide.
267. An isolated peptide according to AE NO 265, wherein the peptide is a cyclized peptide.
268. An isolated peptide according to AE NO 267, wherein the peptide is cyclized using head-to-tail (HTT) cyclization.
269. A molecule comprising an isolated peptide according to any of AE NOs 226-268
20 chemically linked to one or more additional peptide or non-peptide moieties.
270. A molecule according to AE NO 269, wherein the one or more additional peptide or non-peptide moieties improves the production, purification, stability in vitro, stability in vivo, detection, half-life, bioavailability, blood-brain barrier permeation, or activity of the peptide.
- 25 271. An isolated peptide or molecule according to any of AE NOs 226-268 in a salt form.
272. An isolated peptide or molecule according to AE NO 271, wherein the salt is a trifluoroacetic acid (TFA) salt, a sodium salt, a pamoate salt, a chloride salt, or an acetic acid salt.
273. An isolated peptide or molecule according to any of AE NOs 226-268, wherein the
30 peptide has an EC₅₀ for activation of a human delta opioid receptor of < 100 μM.
274. An isolated peptide or molecule according to any of AE NOs 226-268, wherein the peptide has an EC₅₀ for activation of a human delta opioid receptor of < 10 μM.
275. An isolated peptide or molecule according to any of AE NOs 226-268, wherein the peptide has an EC₅₀ for activation of a human delta opioid receptor of < 1 μM.

276. An isolated peptide according to any of AE NOs 226-268, wherein the peptide exhibits at least 50% agonist activity at the human delta opioid receptor at a concentration at or below $< 100 \mu\text{M}$.
277. An isolated peptide according to any of AE NOs 226-268, wherein the peptide exhibits at least 50% agonist activity at the human delta opioid receptor at a concentration at or below $< 10 \mu\text{M}$.
278. An isolated peptide according to any of AE NOs 226-268, wherein the peptide exhibits at least 50% agonist activity at the human delta opioid receptor at a concentration at or below $< 10 \mu\text{M}$.
279. A composition comprising an isolated peptide or molecule according to any of AE NOs 226-268 and one or more additional components.
280. A pharmaceutical composition comprising an isolated peptide or molecule according to any of AE NOs 226-268 and one or more additional components suitable for administration to a mammalian subject.
281. A composition according to AE NO 280 or a pharmaceutical composition according to AE NO 281, wherein the additional components are selected from the group consisting of: pharmaceutically acceptable carriers, excipients, wetting agents, emulsifying agents, pH buffering agents, and preservatives.
282. A nucleic acid molecule that encodes a peptide according to any one of the AE NOs 226-268.
283. A vector comprising a nucleic acid molecule according to AE NO 283.
284. A cell comprising a nucleic acid according to AE NO 283 or a vector according to AE NO 284.
285. A method of activating a delta opioid receptor in vitro or in vivo, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, with an effective amount of a peptide, molecule or composition according to any one of AE NOs 226--282.
286. A method of treating a mammalian subject having a condition amenable to treatment with a delta opioid receptor, the method comprising administering an effective amount of a peptide, molecule, or composition according to any one of AE NOs 226-282, to the subject.
287. A method of treating a mammalian subject having a condition amenable to treatment with a peptide, molecule, or composition according to any one of AE NOs 226-282, the method comprising administering an effective amount of a peptide, molecule, or composition according to any one of AE NOs 226-282, to the subject.

288. A method of treating pain, depression, anxiety, addiction, or substance abuse in a subject in need thereof, the method comprising administering an effective amount of a peptide, molecule, or composition according to any one of AE NOs 226-282, to the subject.
289. A method of treating pain in a subject in need thereof the method comprising
5 administering an effective amount of a peptide, molecule, or composition according to any one of AE NOs 226-282, to the subject.
290. The method of AE NO 286, wherein the condition is pain, depression, anxiety, addiction, or substance abuse.
291. The method of AE NO 286, wherein the condition is pain.
- 10 292. The method of any of AE NOs 7-12, 22-27, 37-42, 52-57, 67-72, 82-87, 97-102, 112-117, 127-132, 142-147, 157-162, 172-177, 187-192, 202-207, 217-222, 286-291, wherein the peptide or composition is administered to the subject orally, subcutaneously, intravenously, intramuscularly, sublingually, or intrathecally.
293. The method of AE NO 292, wherein the peptide or composition is administered to the
15 subject orally.
294. The method of AE NO any one of AE NOs 7-12, 22-27, 37-42, 52-57, 67-72, 82-87, 97-102, 112-117, 127-132, 142-147, 157-162, 172-177, 187-192, 202-207, 217-222, 286-291, 292, or 293, further comprising administering one or more additional active agents to the subject.
- 20 295. The method of AE NO 294, wherein the additional active agent has analgesic properties.
296. The method of AE NO 294, wherein the additional active agent is a mu opioid agonist.
297. The method of AE NO 294, wherein the additional active agent is an NSAID.
298. The method of AE NO 294, wherein the additional active agent is acetaminophen.
299. The method of AE NO 294, wherein additional active agent is probenecid.
- 25 300. The method of any of AE NOs 7-12, 22-27, 37-42, 52-57, 67-72, 82-87, 97-102, 112-117, 127-132, 142-147, 157-162, 172-177, 187-192, 202-207, 217-222, or 286-299, wherein the subject is a non-human primate.
301. The method of any of AE NOs 7-12, 22-27, 37-42, 52-57, 67-72, 82-87, 97-102, 112-117, 127-132, 142-147, 157-162, 172-177, 187-192, 202-207, 217-222, or 286-299,
30 wherein the subject is a human.
302. The method of any of AE NOs 7-12, 22-27, 37-42, 52-57, 67-72, 82-87, 97-102, 112-117, 127-132, 142-147, 157-162, 172-177, 187-192, 202-207, 217-222, or 286-299, wherein the subject is a rodent.
303. In some embodiments, the peptides of the present invention do not induce tolerance and
35 maintain efficacy at the same dose after multiple administrations.

304. In some embodiments, the peptides of the present invention have analgesic efficacy in a non-human primate model of pain.
305. In some embodiments, the peptides of the present invention do not induce preference (an indicator of addiction) in animal models.
- 5 306. An isolated delta opioid receptor agonist peptide, wherein the peptide comprises:
 (a) the amino acid sequence:
 $X_2X_3X_4X_5X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}$,
 wherein, independently of each other:
 X_2 is D, K, or R;
 X_3 is G, K, S, or W;
 X_4 is A, D, F, G, K, W, or Y;
 X_5 is A, C, D, E, G, H, K, N, S, or Y;
 X_6 is A, D, E, G, I, K, L, Q, or V;
 X_7 is A, E, G, I, L, M, V, or W;
 X_8 is A, D, G, S, or V;
 X_9 is A, C, F, H, I, K, L, P, Q, R, T, V, or W;
 X_{10} is A, C, D, E, G, H, K, P, Q, R, V, W, or Y;
 X_{11} is A, E, H, N, Q, or R;
 X_{12} is A, G, L, P, Q, T, or V;
 X_{13} is A, K, P, or S;
 X_{14} is A, F, I, K, L, or Y;
 X_{15} is K, L, P, or V;
 X_{16} is A, K, L, P, or S;
 X_{17} is A, C, D, H, K, N, Q, R, S, or Y;
 X_{18} is A, G, I, K, or V; and
 X_{19} is A, D, F, K, or S, or
 (b) a fragment of the amino acid sequence of part (a), wherein the fragment is from 3-17 amino acids in length, or
 (c) a retro-inverso variant of the amino acid sequence of part (a) or part (b), or
 (d) a variant of the amino acid sequence of part (a), (b), or (c), wherein one or more amino acids is added, deleted, or substituted with a different amino acid, or
 (e) a variant of the amino acid sequence of part (a), (b), (c), or (d) wherein one or more of the amino acids is a modified amino acid.
307. An isolated delta opioid receptor agonist peptide according to AE NO 306, comprising:

- (a) the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315, 438-752 or 747-875, or
- (b) a fragment of the amino acid sequence of part (a), wherein the fragment is from 3-17 amino acids in length, or
- 5 (c) a retro-inverso variant of the amino acid sequence of part (a) or part (b), or
- (d) a variant of the amino acid sequence of part (a), (b), or (c), wherein one or more amino acids is added, deleted, or substituted with a different amino acid, or
- (e) a variant of the amino acid sequence of part (a), (b), (c), or (d) wherein one or more of the amino acids is a modified amino acid.
- 10 308. An isolated delta opioid receptor agonist peptide according to AE NO 306, comprising:
- (a) the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315, or
- (b) a fragment of the amino acid sequence of part (a), wherein the fragment is from 3-17 amino acids in length, or
- (c) a retro-inverso variant of the amino acid sequence of part (a) or part (b), or
- 15 (d) a variant of the amino acid sequence of part (a), (b), or (c), wherein one or more amino acids is added, deleted, or substituted with a different amino acid, or
- (e) a variant of the amino acid sequence of part (a), (b), (c), or (d) wherein one or more of the amino acids is a modified amino acid.
309. An isolated delta opioid receptor agonist peptide according to AE NO 306, comprising:
- 20 the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315, 438-752 or 747-875.
310. An isolated peptide comprising the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315.
311. An isolated peptide comprising the amino acid sequence of any one of PEP NO: and/or
- 25 SEQ ID NO: 16, 17, 24, 86, 87, 157, 162, 163, 164, 165, 166, 167, 170, 171, 173, 175, 177, 178, 179, 182, 183, 185, 186, or 187.
312. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 16.
313. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID
- 30 NO: 17.
314. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 24.
315. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 86.

316. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 87.
317. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 157.
- 5 318. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 162.
319. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 163.
320. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID
10 NO: 164.
321. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 165.
322. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 166.
- 15 323. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 167.
324. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 170.
325. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID
20 NO: 171.
326. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 173.
327. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 175.
- 25 328. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 177.
329. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 178.
330. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID
30 NO: 179.
331. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 182.
332. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 183.

333. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 185.
334. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 186.
- 5 335. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 187.
336. A composition comprising a peptide according to any one of AE NOs 306-335.
337. A composition comprising a peptide according to any one of AE NOs 306-335, and at least one pharmaceutically acceptable carrier or excipient.
- 10 338. A composition comprising a salt of a peptide according to any one of claims AE NOs 306-335.
339. A composition comprising a salt of a peptide according to any one of claims AE NOs 306-335, and at least one pharmaceutically acceptable carrier or excipient.
- 15 340. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to any one of claims AE NOs 306-335.
341. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to AE NO 336.
- 20 342. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to AE NO 337.
343. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to AE NO 338.
- 25 344. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to AE NO 339.
345. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a peptide according to any one of AE NOs 306-335.
- 30 346. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to AE NO 336.
347. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to AE NO 337.
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348. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to AE NO 338.
349. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to AE NO 339.
- 5 350. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a peptide according to any one of AE NOs 306-335.
351. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to AE NO
10 336.
352. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to AE NO 337.
353. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according
15 to AE NO 338.
354. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to AE NO 339.
- 20 355. A composition comprising: an orally active means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
356. A composition comprising: a means for inducing analgesia in a subject, and a pharmaceutically acceptable carrier or excipient.
357. A composition comprising: a means for activating a delta opioid receptor by oral
25 administration to a subject, and a pharmaceutically acceptable carrier or excipient.
358. A composition comprising: a means for inducing analgesia by oral administration to a subject, and a pharmaceutically acceptable carrier or excipient.
359. A composition comprising: a means for activating a delta opioid receptor with an EC₅₀ of at least 10 micromolar, and a pharmaceutically acceptable carrier or excipient.
- 30 360. A composition comprising: a means for inducing analgesia by activating a delta opioid receptor with an EC₅₀ of at least 10 micromolar, and a pharmaceutically acceptable carrier or excipient.
361. A composition comprising: a means for selectively activating a delta opioid receptor in vitro or in vivo, and a pharmaceutically acceptable carrier or excipient.

362. A composition comprising: a means for inducing analgesia by selectively activating a delta opioid receptor in vivo, and a pharmaceutically acceptable carrier or excipient.
363. A composition comprising: a fatty-acid containing means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
- 5 364. A composition comprising: a fatty-acid containing means for inducing analgesia in a subject, and a pharmaceutically acceptable carrier or excipient.
365. A composition comprising: a palmitic-acid containing means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
366. A composition comprising: a palmitic-acid containing means for inducing analgesia in a subject, and a pharmaceutically acceptable carrier or excipient.
- 10 367. A composition comprising: a means for activating a delta opioid receptor in a mammalian subject, and a pharmaceutically acceptable carrier or excipient.
368. A composition comprising: a means for inducing analgesia in a mammalian subject, and a pharmaceutically acceptable carrier or excipient.
- 15 369. A composition comprising: a means for activating a delta opioid receptor in a rodent, and a pharmaceutically acceptable carrier or excipient.
370. A composition comprising: a means for inducing analgesia in a rodent, and a pharmaceutically acceptable carrier or excipient.
371. A composition comprising: a means for activating a delta opioid receptor in a non-human primate, and a pharmaceutically acceptable carrier or excipient.
- 20 372. A composition comprising: a means for inducing analgesia in a non-human primate, and a pharmaceutically acceptable carrier or excipient.
373. A composition comprising: a means for activating a delta opioid receptor in a human subject, and a pharmaceutically acceptable carrier or excipient.
- 25 374. A composition comprising: a means for inducing analgesia in human subject, and a pharmaceutically acceptable carrier or excipient.
375. A composition comprising: a means for activating a delta opioid receptor outside of the central nervous system (CNS), and a pharmaceutically acceptable carrier or excipient.
376. A composition comprising: a means for inducing analgesia by activating a delta opioid receptor outside of the central nervous system (CNS), and a pharmaceutically acceptable carrier or excipient.
- 30 377. A composition comprising: a means for safely activating a delta opioid receptor in a living subject, and a pharmaceutically acceptable carrier or excipient.
378. A composition comprising: a means for safely inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
- 35

379. A composition comprising: a 3-5 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
380. A composition comprising: a 3-5 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
- 5 381. A composition comprising: a 5-10 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
382. A composition comprising: a 5-10 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
383. A composition comprising: a 10-15 amino peptide means for activating a delta opioid
10 receptor, and a pharmaceutically acceptable carrier or excipient.
384. A composition comprising: a 10-15 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
385. A composition comprising: a 15-20 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
- 15 386. A composition comprising: a 15-20 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
387. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to AE NO 355-386.
- 20 388. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to AE NO 355-386.
389. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to AE NO 355-386.
- 25 390. A molecule according to any of Figs. 3-44.

The invention is further described in the following non-limiting Examples.

EXAMPLES

Example 1: In vitro agonist determination using a cAMP assay

30 In vitro DOR agonist activity of each of PEP NOs: and/or SEQ ID NOs: 1-315 was tested using a standard, commercially available cAMP assay (Eurofins DiscoverX HitHunter™ cAMP Assay) using CHO-K1 cells stably expressing the human DOR (cAMP Hunter™ CHO-K1 OPRD1 Gi Cell Line).

In brief, the assay can be summarized as follows:

CHO-K1 cells stably expressing the human DOR (accession NM_000911) were used to monitor the activation of the DOR via Gi cyclic AMP (cAMP) secondary messenger signaling in a gain-of-signal competitive immunoassay using Enzyme Fragment Complementation (EFC) with β -galactosidase (β -Gal) as the functional reporter. In this system, the enzyme is split into two complementary portions: “EA” for Enzyme Acceptor and “ED” for Enzyme Donor. In the assay, ED-labeled cAMP competes with cAMP generated by cells for binding to a cAMP-specific antibody. Active β -Gal is formed by complementation of exogenous EA to any unbound ED-cAMP. Active enzyme can then convert a chemiluminescent substrate, generating an output signal detectable on a standard microplate reader. The addition of EC₈₀ forskolin (approximately 15 μ M) induces a signal and DOR agonists compete to lower the signal.

In brief, the assay was performed as follows:

1. Peptides having the sequences of PEP NOs: and/or SEQ ID NOs: 1-315 (referred to as “test peptides” for the purposes of this Example) were synthesized essentially as described in Example 6, with some differences depending on the specific modifications included in a given peptide (all were synthesized using routine peptide synthesis and modification methodologies).
2. A stock concentration solution of each peptide was prepared by adding to the lyophilized peptide a suitable vehicle (water or DMSO) to achieve a desired stock concentration (typically 10 mM).
3. CHO-K1 cells stably expressing the human DOR were expanded from freezer stocks according to standard procedures. Cells were seeded into 96-well microplates (typically white-walled) to a density of approximately 25,000 cells/well in 100 μ L and incubated at 37°C and 5% CO₂ overnight prior to testing.
4. Intermediate dilutions of test peptide stocks were performed to generate a 100X (a concentration 100 times higher than the desired testing concentration) test peptide sample in vehicle (water or DMSO), and then a 1X test peptide sample in assay buffer (PBS containing 15 μ M forskolin) was prepared.
5. Media was aspirated from cells and replaced with 45 μ L of 1X test peptide sample in assay buffer and then incubated at 37°C for 30 minutes.
6. Following incubation, 15 μ L of cAMP Antibody reagent was added to each well.
7. Then, 60 μ L of working cAMP detection solution (containing 19-parts cAMP lysis buffer, 5-parts substrate reagent 1, 1-part substrate reagent 2, and 25-parts cAMP solution D) was added and incubated for one hour in the dark at room temperature.

8. Then, 60 µL cAMP solution A was added and incubated for 1-3 hours at room temperature in the dark.
9. Last, microplates were read following signal generation with a PerkinElmer Envision, Promega GloMax, Molecular Devices ID3, or other comparable instrument for
- 5 chemiluminescent signal detection.

Percentage activity (or percent activity of control agonist response) was calculated using the formula:

$$\% \text{ activity} = 100\% \times \left(1 - \frac{(\text{mean RLU test peptide}) - (\text{mean RLU positive control})}{(\text{mean RLU vehicle control}) - (\text{mean RLU positive control})} \right)$$

- where the positive control was DPDPE ([D-Pen2,5]-Enkephalin,) at 10 nM and RLU refers to
- 10 relative luminescence units (an arbitrary unit of luminescence as reported by the instrument for chemiluminescent signal detection).

Each of PEP NOs: and/or SEQ ID NOs: 1-315 exhibited delta opioid receptor agonist activity of at least 50% at or below 100 µM in this assay. The % activity demonstrated by each of these peptides at 100 µM is shown in Table 3 (above).

- 15 Representative agonist response curves for one peptide are shown in **Fig. 2A**, which shows an in vitro agonist response curve for a test peptide having the amino sequence of PEP NO: and/or SEQ ID NO: 157 – as obtained using this fluorescent cAMP assay.

- This same assay is performed to demonstrate and/or confirm DOR induced cAMP activity at one or more concentrations of any peptide of the present invention including but not limited to those
- 20 having the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 1-315 or 438-752, or those comprising the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 747-875, or peptides having a consensus sequence comprising the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 316-437.

Example 2: In vitro agonist determination using a calcium flux assay

- 25 In vitro DOR agonist activity of a subset of the peptides of the invention was tested using a standard, commercially available calcium flux assay. This assay provides for the evaluation of the agonist activity of compounds at the human delta (DOP) receptor expressed in rat basophil leukemia cells, determined by measuring their effect on cytosolic calcium ion (Ca²⁺) mobilization using a fluorimetric detection method.
- 30 Peptides of the present invention (referred to as “test peptides” for the purposes of this Example) were synthesized essentially as described in Example 6, with some differences depending on the

specific modifications included in a given peptide (all peptides are synthesized using routine peptide synthesis and modification methodologies). The test peptides were prepared as stock solutions in water or DMSO.

In brief, the assay was performed as follows:

- 5 1. The cells suspended in HBSS buffer (Invitrogen) complemented with 20 mM Hepes then distributed in microplates at a density of 2.768×10^4 cells/well.
2. The fluorescent probe (Fluo8, AAT Bioquest) mixed with probenidicid in HBSS buffer (Invitrogen) complemented with 20 mM Hepes (Milipore) (pH 7.4) was then added into each well and equilibrated with the cells for 60 min at 30°C.
- 10 3. Thereafter, the assay plates were positioned in a microplate reader (FlipR Tetra, Molecular Device) which was used for the addition of the test compound, reference agonist or HBSS buffer (basal control), and the measurements of changes in fluorescence intensity which varies proportionally to the free cytosolic Ca^{2+} ion concentration.
4. For stimulated control measurements, DPDPE at 1 μM was added in separate assay wells.
- 15 5. The results were expressed as a percent of the control response to DPDPE at 1 μM .
6. The standard reference agonist was DPDPE, which was tested in each experiment at several concentrations to generate a concentration-response curve from which its EC50 value was calculated.

20 A subset of the peptides of the present invention was tested in the assay of this Example, and the results for those peptides producing inhibition (as a percent of the control response to DPDE at 1 μM) of at least 50% are shown in Table 4. Table 4 provides the lowest tested molar concentration (M) for each listed peptide at which >50% inhibition of control was observed, as well as the inhibition as a percent of control at that concentration.

Table 4. DOR agonism as demonstrated by calcium flux assay results

PEP NO: and/or SEQ ID NO:	Lowest concentration at which >50% inhibition of control was observed (M)	% inhibition of control at lowest concentration at which >50% inhibition of control was observed
1	2.0E-05	60%
2	2.0E-05	63%
3	2.0E-05	78%
5	2.0E-05	57%
6	2.0E-05	75%
7	2.0E-05	84%
8	2.0E-05	70%
9	2.0E-05	58%
10	2.0E-05	68%
11	2.0E-05	87%
12	2.0E-05	81%
14	2.0E-05	71%
15	2.0E-05	86%
16	2.0E-05	93%
17	2.0E-05	67%
23	1.0E-05	50%
24	3.0E-07	67%

PEP NO: and/or SEQ ID NO:	Lowest concentration at which >50% inhibition of control was observed (M)	% inhibition of control at lowest concentration at which >50% inhibition of control was observed
28	2.0E-05	66%
29	2.0E-05	59%
33	2.0E-05	58%
37	2.0E-05	52%
38	2.0E-05	60%
42	2.0E-05	65%
45	5.0E-06	65%
46	2.0E-05	63%
53	2.0E-05	67%
54	2.0E-05	72%
55	2.0E-05	78%
56	2.0E-05	72%
57	2.0E-05	64%
58	2.0E-05	81%
59	5.0E-06	52%
60	2.0E-05	56%
65	2.0E-05	73%
66	5.0E-06	58%
67	2.0E-05	54%
68	5.0E-06	55%
69	2.0E-05	69%
70	2.0E-05	75%
71	2.0E-05	70%
79	2.0E-05	57%
80	2.0E-05	55%
82	2.0E-05	73%
83	2.0E-05	65%

Representative agonist response curves for one peptide are shown in **Fig. 2B**, which shows an in vitro agonist response curve for a test peptide having the amino sequence of PEP NO: and/or SEQ ID NO: 24 – as obtained using this fluorescent cAMP assay.

- 5 This same assay is performed to demonstrate and/or confirm DOR induced calcium flux activity at one or more concentrations of any peptide of the present invention including but not limited to those having the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 1-315 or 438-752, or those comprising the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 747-875, or peptides having a consensus sequence comprising the amino acid sequences of PEP NOs: and/or
- 10 SEQ ID NOs: 316-437.

Example 3: In vitro DOR binding determination via competitive radioligand assay

- Example 1, above, provides data demonstrating that peptides of the present invention have DOR agonist activity. In this Example we provide data from an in vitro competitive binding assay. In vitro binding of a subset of the peptides of the present invention was confirmed using a
- 15 competitive radioligand assay in which the ability of test peptides to compete with a known DOR agonist (the synthetic delta opioid receptor agonist [D-Ala2, D-Leu5]-Enkephalin or “DADLE”) for DOR binding was assessed. The assay was performed as follows.

Peptides (referred to as “test peptides” for the purposes of this Example) were synthesized essentially as described in Example 6, with some differences depending on the specific

modifications included in a given peptide (all were synthesized using routine peptide synthesis and modification methodologies). The test peptides were initially prepared as 100X stock solutions in water or DMSO.

Cell membrane homogenates (about 1 µg protein) from rat basophilic leukemia cells (transfected to overexpress the human DOR receptor) were incubated for 60 minutes at 22°C with 0.5 nM of radiolabeled (tritiated [³H]) DADLE in the absence or presence of the 1X test peptide in a buffer containing 50 mM Tris-HCl (pH 7.4) and 5 mM MgCl₂. Incubations were performed in a total volume of 200 µL in a 96-well plate. Following incubation, the samples were filtered rapidly under vacuum through glass fiber filters (GF/B, Packard) presoaked with 0.3% polyethylenimine ("PEI") and rinsed several times with ice-cold 50 mM Tris-HCl using a 96-sample cell harvester. The filters were dried and then radioactivity levels were counted in a scintillation counter (Topcount, Packard) using a scintillation cocktail (Microscint 0, Packard).

Nonspecific binding was determined in the presence of 10 µM naltrexone. Control specific binding was determined as (a) the maximal signal as determined in wells containing receptor and radioligand (0.5 nM of radiolabeled (tritiated [³H]) DADLE) minus (b) the minimal signal as determined in wells containing a high concentration of unlabeled competitor (10 µM naltrexone) added to receptor and radioligand.

Binding of test peptides was calculated as % inhibition of the binding of the radioactively labeled DADLE:

$$100 \times \frac{\text{measured specific binding}}{\text{control specific binding}}$$

and as a percent inhibition of control specific binding:

$$100 - \left(100 \times \frac{\text{measured specific binding}}{\text{control specific binding}} \right)$$

As obtained in the presence of the specified test peptide.

A subset of PEP NOs: and/or SEQ ID NOs: was tested in the assay of this Example and the results for those with a result (inhibition as a percent of the control response) of at least 50% are shown in Table 5. Table 5 provides the lowest tested molar concentration (M) at which >50% inhibition of control was observed as well as the inhibition as a percent of control at that concentration.

Table 5. DOR radioligand binding assay results

PEP NO: and/or SEQ ID NO:	Lowest concentration at which >50% inhibition of control specific binding was observed (M)	% inhibition of control at lowest concentration at which >50% inhibition of control specific binding was observed
1	1.0E-05	55%
24	1.0E-06	101%
157	3.2E-08	78%
162	1.0E-06	59%
163	1.0E-05	87%
173	1.0E-07	85%

Representative results are also shown in **Fig. 2C**, which shows a binding curve for a test peptide having the amino sequence of PEP NO: and/or SEQ ID NO: 157 - as obtained using this competitive radioligand assay.

This same assay is performed to demonstrate and/or confirm DOR binding and/or DOR binding affinity for any of the peptides of the present invention (including but not limited to PEP NOs: and/or SEQ ID NOs: 1-315, 438-752, or 747-875) at any desired concentration.

Example 4: Additional In vitro agonist assays

Example 1 and Example 2 above describe experiments performed that demonstrate DOR agonist activity of peptides of the present invention using a cAMP production assay and a calcium flux assay, respectively. This Example describes other in vitro assays that can be used to confirm DOR agonism of any of the peptides of the present invention, including, but not limited to those having the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 1-315 or 438-752, or those comprising the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 747-875, or peptides having a consensus sequence comprising the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 316-437.

Peptides of the present invention (referred to as “test peptides” for the purposes of this Example) are synthesized essentially as described in Example 6, with some differences depending on the specific modifications included in a given peptide (all peptides are synthesized using routine peptide synthesis and modification methodologies). The test peptides are prepared as stock solutions in water or DMSO.

Assays are performed to confirm beta arrestin activity of test peptides and a control DOR agonist (such as DADLE) at any desired concentrations using a beta arrestin assay, such as the Eurofins DiscoverX PathHunter® β -Arrestin Assay (as described in the DiscoverX PathHunter® β -Arrestin Assay for GPCR Cell Lines User Manual) in combination with appropriate DOR expressing cells.

Assays are performed to confirm DOR agonist activity of test peptides and one or more control DOR agonists at any desired concentrations using an in vitro receptor internalization assay, such as the Eurofins DiscoverX PathHunter® Activated GPCR Internalization Assay (as described in the Eurofins DiscoverX PathHunter® Activated GPCR Internalization Assay User Manual) in
5 combination with appropriate DOR expressing cells.

Example 5: Analgesia in rodent model of pain

Peptides of the present invention (referred to as “test peptides” for the purposes of this Example) were synthesized essentially as described in Example 6, with some differences depending on the specific modifications included in a given peptide (all peptides are synthesized using routine
10 peptide synthesis and modification methodologies).

The analgesic effect of 24 test peptides was assessed in two species of rodents (mice and rats) using a hot plate assay designed to measure the response of a mouse or rat to a painful hot temperature, as described below. The 24 peptides selected for testing in this assay were selected based on their diversity of structure, size, length, and sequence to confirm that an ability to elicit
15 in vivo analgesia is not unique to one peptide or one group of the peptides of the present invention but rather is a general property that spans, and is representative of, the full scope of the genus of peptides invented.

Rodents were placed on a metal plate heated to a temperature of 55°C (as verified using an infrared (IR) thermometer). Rodents were allowed to stay on the hotplate for a maximum of
20 30 seconds, thus preventing the possibility of tissue damage. As soon as a behavioral response indicating pain in a rodent was observed (e.g., flinching of the rear foot or licking of the rear paws or an escape response) the experiment was stopped by removing the rodent from the device. The amount of time each rodent spent on the hot plate was recorded. Hot plate tests were performed prior to administration of test peptide and again at one or more timepoints after
25 administration. The time (in seconds) spent on the hot plate at a given timepoint after administration minus the time spent on the hot plate prior to administration is referred to herein as the “time difference from baseline.”

A subset of 24 of the peptides listed in Table 3 was tested (the PEP NOs: and/or SEQ ID NOs: of these peptides are provided in Table 6 below). These test peptides (dissolved in a vehicle of
30 water, 0.9% NaCl, or 0.5% carboxymethyl cellulose) were administered to rodents over a range of doses and using several administration routes (intravenous (IV), subcutaneous (SC), and oral (PO)). As controls, rodents were treated with vehicle only (i.e., vehicle with no peptide, administered using the same route as the test peptides). All 24 of the peptides tested produced an

analgesic effect - exhibiting an increase in reaction time (delayed reaction) of at least 5%, as compared to the pre-dose reaction time, at one or more timepoints after dosing. A threshold of at least 5% is considered significant as placebo controls often demonstrate significant decreases in reaction time (faster reaction), as compared to the pre-dose reaction time, at one or more timepoints after dosing (suggesting hypersensitization and/or learned avoidance). The data from this study is provided in Table 6, below. The rodent species tested are listed in Table 6 and were wild-type rodents.

Table 6. Analgesic effect in rodent models of pain

PEP NO: and/or SEQ ID NO:	Approximate dose. (mg/kg)	Administration route	Species	Maximal change from baseline (%)	Timepoint at which maximal analgesic effect was observed	Last timepoint of analgesic effect	Change from baseline (%) at last timepoint of analgesic effect
16	160	SC	mouse	31%	30 min	300 min	12%
17	160	SC	mouse	25%	60 min	90 min	14%
24	80	IV	mouse	76%	10 min	90 min	36%
24	800	PO	mouse	143%	180 min	300 min	57%
24	600	SC	mouse	122%	60 min	25 hr	78%
24	168	SC	rat	55%	60 min	300 min	13%
86	600	PO	mouse	69%	60 min	180 min	13%
86	160	SC	mouse	206%	90 min	300 min	130%
87	600	PO	mouse	15%	90 min	90 min	15%
157	1000	PO	mouse	117%	180 min	180 min	32%
157	1000	PO	rat	100%	180 min	300 min	6%
157	160	SC	mouse	154%	90 min	300 min	54%
157	300	SC	rat	102%	180 min	180 min	102%
162	800	PO	mouse	38%	60 min	120 min	18%
162	160	SC	mouse	145%	90 min	300 min	84%
163	160	SC	mouse	95%	120 min	300 min	63%
164	160	SC	mouse	12%	90 min	90 min	12%
165	160	SC	mouse	5%	60 min	60 min	5%
166	160	SC	mouse	40%	90 min	120 min	37%
167	160	SC	mouse	45%	90 min	300 min	10%
170	800	PO	mouse	53%	90 min	180 min	37%
171	800	PO	mouse	51%	90 min	300 min	16%
173	800	PO	mouse	60%	90 min	300 min	16%
173	160	SC	mouse	69%	60 min	300 min	7%
175	800	PO	mouse	41%	60 min	180 min	19%
177	800	PO	mouse	14%	60 min	90 min	13%
178	800	PO	mouse	88%	90 min	300 min	19%
178	160	SC	mouse	85%	60 min	180 min	25%
179	800	PO	mouse	109%	90 min	300 min	46%
179	160	SC	mouse	81%	90 min	180 min	41%
182	400	SC	mouse	150%	90 min	300 min	58%
183	800	PO	mouse	29%	90 min	300 min	7%
185	800	PO	mouse	74%	180 min	300 min	20%
186	800	PO	mouse	40%	180 min	300 min	19%
187	800	PO	mouse	108%	90 min	300 min	64%

Importantly, this data demonstrates that the in vitro DOR agonist activity of the peptides of the invention described above translates to in vivo efficacy in treatment of pain. Furthermore, the fact that all 24 of the peptides tested in this experiment exhibited analgesic activity in vivo is very significant because it demonstrates that analgesic activity is not a property of just a subset of the peptides of the present invention that exhibit a high degree of sequence identity. Rather, our results demonstrate that analgesic activity is a shared biological property of the peptides of

the present invention even though the peptides vary significantly in terms of size, length, modifications, and sequence.

Furthermore, as illustrated by the PO administration results in Table 6, peptides of the present invention exhibit oral efficacy as analgesic agents. This is important because it provides a significant advantage over peptides that require parenteral administration or direct central nervous system administration.

Additionally, peptides of the present invention exhibit a duration of efficacy lasting to at least 60 minutes, or in some cases at least 90 minutes, or in some cases at least 120 minutes, or in some cases at least 180 minutes, or in some cases at least 300 minutes, or in some cases at least 25 hours after dosing (see Table 6). This provides a significant advantage over peptides that have a shorter demonstrated duration of action.

Furthermore, administration of the peptides of Table 6 was not observed to be associated with seizures or convulsions or other side effects observed with other DOR agonists.

This same assay is performed to confirm the analgesic efficacy of any peptides of the present invention at any desired test dose.

Example 6: Production of Peptides & Peptide-Containing Compositions

The peptides of the present invention were identified using a proprietary method designed to identify DOR agonist peptides.

This Example describes the methods that were used to produce and formulate peptides having the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 1-315. However, the same methods, as well as other methods known in the art, can be used to produce and formulate all of the peptides of the present invention.

Peptides having the amino acid sequences of PEP NOs: and/or SEQ ID NOs: 1-315 were synthesized using standard solid phase peptide synthesis methods including those in which peptides were anchored by their C-terminus to an insoluble polymer resin enabling the successive addition of protected amino acids constituting the sequence of the peptide being synthesized. In this process each amino acid was added successively by cleavage of a protecting group and then coupling of the next protected amino acid in the sequence, with washing steps in between. The system used was an Fmoc-based solid phase synthesis system including fluorenylmethoxycarbonyl (Fmoc) protecting groups and treatments with piperidine, dimethylformamide (DMF), 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), 1-Hydroxybenzotriazole (HOBt), and/or 1-hydroxy-7-aza-benzotriazole (HOAt) among other

reagents known in the art. Once completed, the peptides were cleaved from the resin and subjected to further washing, purification, salt exchange, lyophilization, and characterization as necessary.

For those peptides that contain modified amino acids, or other modifications, modifications were either introduced following methods commonly known in the art or were already present in the amino acid being incorporated.

For some peptides, {dβD} was incorporated using Fmoc-D-Asp-OtBu or CAS#134098-70-7. For some peptides {n-peg40k-} was incorporated using PEG40K-NHS. For some peptides {r-peg40k-} as conjugated to a cysteine was incorporated using PEG40K-Maleimide. For some peptides {r-peg40k-} was incorporated using mPEG-dibenzocyclooctyne (mPEG-DBCO), with an average molecular weight of 40 kDa, and a lysine-azide (as for {{r-peg40k-dbco}-{azide-K}}).

Table 7 below provides further details of one protocol used to synthesize some of the peptides of the present invention. In Table 7 “AA#C-term” refers to the C-terminal amino acid, “AA#C-term-1” refers to the amino acid immediately adjacent to the C-terminal amino acid toward the N-terminus, and “AA#1” refers to the N-terminal amino acid. In Table 7, Stage III describes a palmitoylation step that was used in certain peptides requiring such palmitoylation step (e.g., PEP NO: and/or SEQ ID NO: 24, 42, 86, 157, and is used for other sequences containing an {r-pal-K} or {r-pal-{dK}}). In Table 7, Stage IV describes a purification, salt-exchange, and lyophilization step which was done to produce a sodium salt composition. In Table 7 the Monitoring column describes several assays that were performed during synthesis to monitor the synthesis. In Table 7 abbreviations of chemicals are used as is common in the art. In Table 7 amounts of chemicals are as appropriate and/or as commonly used in the art.

Table 7. Method of peptide synthesis

Stage / Step	Description	Monitoring
Stage I: Solid phase assembling of peptide chain		
Step 1: Deprotection of Fmoc group and coupling of AA#C-term	1 – Swell and wash with DMF	Kaiser and TNBS tests to monitor Fmoc deprotection. Kaiser and TNBS test to monitor coupling reaction. If positive, recoupling with Fmoc-AA-OH/HOBt/DIC in DMF
	2 – Treatment with Piperidine/DBU/HOBt/DMF twice	
	3 – Washes with DMF, MeOH, DMF	
	4 – Coupling with preactivated Fmoc-AA-OH/HOBt/DIC in DMF	
	5 – Washes with MeOH, DMF	
Step 2: Deprotection of Fmoc group and coupling cycles of AA#C-term-1 to AA#1	1 – Perform the same coupling and deprotection procedure as that of AA#C-term.	Kaiser and TNBS tests or Kaiser and Chloranil tests to detect amine resins to monitor Fmoc deprotection and coupling reaction. If recoupling is required, perform the same coupling procedure as the first coupling for a specific amino acid.
	- For the secondary amine resin, additional 0.1M Oxyma/DMF was used required after Fmoc deprotection	
	- For certain cycle(s), coupling with in-situ activated Fmoc-AA-OH/HOBt/DIC in DMF	
	- As required, for AA#1 or others, the coupling reagent of HOBt is replaced with HOAt	
Stage II:	2 – Final washes with DMF, MeOH, and DCM	
	3 – Drying under vacuum	
	1 – Treatment with TFA/TIS/H ₂ O	
	2 – Filtration	

Cleavage of peptide resin	3 – Precipitation in MTBE 4 – Filtration and washing with MTBE, heptane 5 – Final drying under vacuum	
Stage III: Palmitoylation	1 – Palm-OSu, DIPEA in DMF 2 – Precipitation with MTBE 3 – Isolation and wash with MTBE and EtOAc 4 – Drying under vacuum	In-process control (“IPC”) HPLC to monitor the Palmitoylation
Stage IV: Purification, Salt-exchange, and Lyophilization	1 – Purification and salt-exchange with 0.1M NaHCO ₃ /ACN/water buffer system 2 – Load the main pool to HPLC column 3 – Elute the peptide radiantly with CAN/water	IPC HPLC to monitor the Purification and Salt-exchange.

Head-to-tail cyclic peptides were synthesized using a method in which the initial steps were conducted in a similar manner to that described above for linear peptide synthesis. Linear peptides were cleaved off the resin, with protection groups remaining on the side chain.

- 5 Subsequently, the linear peptides were cyclized by condensation of the C-terminal carboxyl group and the N-terminal amino group. Side chain protection groups were then removed to yield the cyclic peptide.

Following synthesis, peptides were purified and lyophilized. Lyophilized peptides were stored under appropriate conditions until use such as at less than negative 15 degrees Celsius.

- 10 Lyophilized peptides were reconstituted in appropriate diluents as needed for use. For example, lyophilized peptides were generally reconstituted in water (or other aqueous solution such as normal saline) where solubility permitted or in DMSO. For administration to living subjects, the peptides were prepared (either directly from the lyophilized form or from a stock solution) such that the composition to be administered contained an appropriate concentration of the peptide.

15 **Example 7: Stability of peptides**

This Example describes studies used to determine the stability of the peptides of the present invention.

- Some studies were performed using an HPLC-based assay in which a decrease in purity resulting from the generation of degradation products was observed as a decrease in HPLC % area of the retention time of the peptide. In such assays, the smaller the decrease in HPLC % area, the more stable the peptide is. Table 8 describes 4 stability conditions that were evaluated and provides results for a peptide where a peptide’s purity is compared under certain conditions to a control not subjected to the conditions. The very low decrease in HPLC % area indicated stability of the peptide in all conditions tested.
- 20

Table 8. Stability conditions and results for PEP NO: and/or SEQ ID NO: 157

Condition category	Condition description	HPLC % area change from control
Heat solid	10 mg heated in an oven at about 110°C for about 24 hours	-3.34%
Acid solution	10 mg left in a flask with 2 mL diluent and 1 mL of 1N HCl for about 7 hours at room temperature then neutralized by adding 1 mL of 1N NaOH	-2.17%
Peroxide solution	10 mg left in a flask with 2 mL diluent and 1 mL of 3% hydrogen peroxide for 6 hours room temperature	+0.29%
Ultraviolet light solid	10 mg exposed to 200 Watt hrs/m ² of ultraviolet light	-0.76%

Stability may also be evaluated by keeping the peptide at a set temperature for an extended period of time. In the case of PEP NO: and/or SEQ ID NO: 157, storage in lyophilized powder form at 25°C for 6 months resulted in confirmation of stability with a decrease in purity of only 0.4% over the course of the 6 months.

Stability may also be evaluated by keeping the peptide in solution for an extended period of time at various temperatures. In the case of PEP NO: and/or SEQ ID NO: 157, storage in solution with water resulted in confirmation of stability at all conditions tested in Table 9. Table 9 shows the evaluated concentration in mg/mL (in water) at 2 concentrations expressed as a percentage of the starting concentration prior to the timed study.

Table 9. Additional stability conditions and results for PEP NO: and/or SEQ ID NO: 157

Condition tested	Concentration of 20 mg/mL	Concentration of 200 mg/mL
18 hours at about 4°C	100%	100%
10 days at about 4°C	100%	100%
2 hours at about 80°C	98%	98%
24 hours at about 50°C	99%	99%
11 days at about 50°C	97%	95%
24 hours at about 20-25°C	99%	100%
11 days at about 4°C	102%	96%
11 days at about -20°C	101%	101%

Stability may also be evaluated based on the ability of a peptide to maintain its biological activity in vitro, which may be studied, for example, by evaluation in a cAMP assay as described in Example 1. In the case of PEP NO: and/or SEQ ID NO: 157, an evaluation was performed following about 3 years of storage in solution with water at about 20-25°C, and no decrease in cAMP activity or EC₅₀ was observed outside of normal assay variances.

Similarly, the ability of a peptide to maintain its biological activity in vivo may also be studied, such as by evaluation in an analgesia model as described in Example 5. In the case of PEP NO: and/or SEQ ID NO: 157, an evaluation was performed following storage for 1 hour at 20-25°C, 70°C, and 100°C. Under all 3 conditions, an analgesic effect was observed, as indicated in Table 10 which is presented using headings as described in Example 5.

Table 10. Analgesic efficacy following elevated temperature (all by PO administration route)

PEP NO: and/or SEQ ID NO:	Approximate dose, (mg/kg)	Storage condition of peptide in solution of 0.9% NaCl	Species	Maximal change from baseline (%)	Timepoint at which maximal analgesic effect was observed	Last timepoint of analgesic effect	Change from baseline (%) at last timepoint of analgesic effect
157	464	1 hour at 100°C	mouse	17%	90 min	180 min	5%
157	464	1 hour at 70°C	mouse	54%	90 min	180 min	33%
157	464	1 hour at 20-25°C	mouse	69%	90 min	180 min	55%

This same assay is performed to confirm the stability of any peptides of the present invention.

Example 8: Biased DOR agonism

- 5 Biased DOR agonism of a peptide of the present invention was evaluated for PEP NO: and/or SEQ ID NO: 24 by comparing its EC₅₀ or maximum response in a receptor internalization assay or beta arrestin assay to its EC₅₀ or maximum response in a cAMP assay.

A DOR agonist bias factor is determined by dividing the EC₅₀ results to be compared and/or the maximum response results to be compared. A DOR agonist bias factor in excess of 1x indicates a
10 biased DOR agonist.

As shown by the data in Table 11, PEP NO: and/or SEQ ID NO: 24 is a biased DOR agonist, because this peptide preferentially activates cAMP production with a 11x lower EC₅₀ than for receptor internalization and a 59x lower EC₅₀ than for beta arrestin recruitment as well as
15 because this peptide produces a stronger cAMP maximal response 2x that of receptor internalization and a 2x that of beta arrestin recruitment. The maximum response was calculated as a percentage of a positive control response and all assays are performed at the DOR.

Table 11. Biased DOR agonism

PEP NO: and/or SEQ ID NO:	DOR agonist assay	EC ₅₀	Maximum response	EC ₅₀ bias factor vs cAMP (multiple of cAMP EC ₅₀)	Maximum response bias factor vs cAMP (multiple of cAMP maximum response)
24	Internalization	0.065 μ M	57.0%	11x	0.5x
24	Beta arrestin	0.352 μ M	62.0%	59x	0.5x
24	cAMP	0.006 μ M	113.9%		

This same assay is performed to confirm the level of biased DOR agonism of any peptides of the
20 present invention.

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CLAIMS

We claim:

1. An isolated delta opioid receptor agonist peptide, wherein the peptide comprises:
 - (a) the amino acid sequence:

5 X₂X₃X₄X₅X₆X₇X₈X₉X₁₀X₁₁X₁₂X₁₃X₁₄X₁₅X₁₆X₁₇X₁₈X₁₉,

wherein, independently of each other:

X₂ is D, K, or R;

X₃ is G, K, S, or W;

X₄ is A, D, F, G, K, W, or Y;

10 X₅ is A, C, D, E, G, H, K, N, S, or Y;

X₆ is A, D, E, G, I, K, L, Q, or V;

X₇ is A, E, G, I, L, M, V, or W;

X₈ is A, D, G, S, or V;

X₉ is A, C, F, H, I, K, L, P, Q, R, T, V, or W;

15 X₁₀ is A, C, D, E, G, H, K, P, Q, R, V, W, or Y;

X₁₁ is A, E, H, N, Q, or R;

X₁₂ is A, G, L, P, Q, T, or V;

X₁₃ is A, K, P, or S;

X₁₄ is A, F, I, K, L, or Y;

20 X₁₅ is K, L, P, or V;

X₁₆ is A, K, L, P, or S;

X₁₇ is A, C, D, H, K, N, Q, R, S, or Y

X₁₈ is A, G, I, K, or V; and

X₁₉ is A, D, F, K, or S, or
 - 25 (b) a fragment of the amino acid sequence of part (a), wherein the fragment is from 3-17 amino acids in length, or
 - (c) a retro-inverso variant of the amino acid sequence of part (a) or part (b), or
 - (d) a variant of the amino acid sequence of part (a), (b), or (c), wherein one or more amino acids is added, deleted, or substituted with a different amino acid, or
 - 30 (e) a variant of the amino acid sequence of part (a), (b), (c), or (d) wherein one or more of the amino acids is a modified amino acid.
2. An isolated delta opioid receptor agonist peptide according to claim 1, comprising:
 - (a) the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315, 438-752 or 747-875, or

- (b) a fragment of the amino acid sequence of part (a), wherein the fragment is from 3-17 amino acids in length, or
- (c) a retro-inverso variant of the amino acid sequence of part (a) or part (b), or
- (d) a variant of the amino acid sequence of part (a), (b), or (c), wherein one or more amino acids is added, deleted, or substituted with a different amino acid, or
- (e) a variant of the amino acid sequence of part (a), (b), (c), or (d) wherein one or more of the amino acids is a modified amino acid.
3. An isolated delta opioid receptor agonist peptide according to claim 1, comprising:
- (a) the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315, or
- (b) a fragment of the amino acid sequence of part (a), wherein the fragment is from 3-17 amino acids in length, or
- (c) a retro-inverso variant of the amino acid sequence of part (a) or part (b), or
- (d) a variant of the amino acid sequence of part (a), (b), or (c), wherein one or more amino acids is added, deleted, or substituted with a different amino acid, or
- (e) a variant of the amino acid sequence of part (a), (b), (c), or (d) wherein one or more of the amino acids is a modified amino acid.
4. An isolated delta opioid receptor agonist peptide comprising the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315, 438-752 or 747-875.
5. An isolated peptide comprising the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 1-315.
6. An isolated peptide comprising the amino acid sequence of any one of PEP NO: and/or SEQ ID NO: 16, 17, 24, 86, 87, 157, 162, 163, 164, 165, 166, 167, 170, 171, 173, 175, 177, 178, 179, 182, 183, 185, 186, or 187.
7. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 16.
8. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 17.
9. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 24.
10. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 86.
11. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 87.
12. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 157.

13. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 162.
14. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 163.
- 5 15. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 164.
16. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 165.
17. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 166.
- 10 18. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 167.
19. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 170.
- 15 20. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 171.
21. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 173.
22. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 175.
- 20 23. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 177.
24. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 178.
- 25 25. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 179.
26. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 182.
27. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 183.
- 30 28. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 185.
29. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 186.

30. An isolated peptide comprising the amino acid sequence of PEP NO: and/or SEQ ID NO: 187.
31. A composition comprising a peptide according to any one of claims 1-30.
32. A composition comprising a peptide according to any one of claims 1-30, and at least one pharmaceutically acceptable carrier or excipient.
33. A composition comprising a salt of a peptide according to any one of claims 1-30.
34. A composition comprising a salt of a peptide according to any one of claims 1-30, and at least one pharmaceutically acceptable carrier or excipient.
35. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a peptide according to any one of claims 1-30.
36. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to claim 31.
37. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to claim 32.
38. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to claim 33.
39. A method of activating a delta opioid receptor, the method comprising contacting a delta opioid receptor, or a cell comprising a delta opioid receptor, in vitro or in vivo with a composition according to claim 34.
40. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a peptide according to any one of claims 1-30.
41. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to claim 31.
42. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to claim 32.
43. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to claim 33.
44. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to claim 34.

45. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a peptide according to any one of claims 1-30.
46. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to claim 31.
47. A method of treating pain in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to claim 32.
48. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to claim 33.
49. A method of activating a delta opioid receptor in a subject in need thereof, the method comprising administering to the subject a composition according to claim 34.
50. A composition comprising: a means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
51. A composition comprising: a means for inducing analgesia in a subject, and a pharmaceutically acceptable carrier or excipient.
52. A composition comprising: a means for activating a delta opioid receptor by oral administration to a subject, and a pharmaceutically acceptable carrier or excipient.
53. A composition comprising: a means for inducing analgesia by oral administration to a subject, and a pharmaceutically acceptable carrier or excipient.
54. A composition comprising: a means for activating a delta opioid receptor with an EC₅₀ of at least 10 micromolar, and a pharmaceutically acceptable carrier or excipient.
55. A composition comprising: a means for inducing analgesia by activating a delta opioid receptor with an EC₅₀ of at least 10 micromolar, and a pharmaceutically acceptable carrier or excipient.
56. A composition comprising: a means for selectively activating a delta opioid receptor in vitro or in vivo, and a pharmaceutically acceptable carrier or excipient.
57. A composition comprising: a means for inducing analgesia by selectively activating a delta opioid receptor in vivo, and a pharmaceutically acceptable carrier or excipient.
58. A composition comprising: a fatty-acid containing means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
59. A composition comprising: a fatty-acid containing means for inducing analgesia in a subject, and a pharmaceutically acceptable carrier or excipient.
60. A composition comprising: a palmitic-acid containing means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.

61. A composition comprising: a palmitic-acid containing means for inducing analgesia in a subject, and a pharmaceutically acceptable carrier or excipient.
62. A composition comprising: a means for activating a delta opioid receptor in a mammalian subject, and a pharmaceutically acceptable carrier or excipient.
- 5 63. A composition comprising: a means for inducing analgesia in a mammalian subject, and a pharmaceutically acceptable carrier or excipient.
64. A composition comprising: a means for activating a delta opioid receptor in a rodent, and a pharmaceutically acceptable carrier or excipient.
65. A composition comprising: a means for inducing analgesia in a rodent, and a
10 pharmaceutically acceptable carrier or excipient.
66. A composition comprising: a means for activating a delta opioid receptor in a non-human primate, and a pharmaceutically acceptable carrier or excipient.
67. A composition comprising: a means for inducing analgesia in a non-human primate, and a pharmaceutically acceptable carrier or excipient.
- 15 68. A composition comprising: a means for activating a delta opioid receptor in a human subject, and a pharmaceutically acceptable carrier or excipient.
69. A composition comprising: a means for inducing analgesia in human subject, and a pharmaceutically acceptable carrier or excipient.
70. A composition comprising: a means for activating a delta opioid receptor outside of the
20 central nervous system (CNS), and a pharmaceutically acceptable carrier or excipient.
71. A composition comprising: a means for inducing analgesia by activating a delta opioid receptor outside of the central nervous system (CNS), and a pharmaceutically acceptable carrier or excipient.
72. A composition comprising: a means for safely activating a delta opioid receptor in a
25 living subject, and a pharmaceutically acceptable carrier or excipient.
73. A composition comprising: a means for safely inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
74. A composition comprising: a 3-5 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
- 30 75. A composition comprising: a 3-5 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
76. A composition comprising: a 5-10 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
77. A composition comprising: a 5-10 amino peptide means for inducing analgesia in a living
35 subject, and a pharmaceutically acceptable carrier or excipient.

78. A composition comprising: a 10-15 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
79. A composition comprising: a 10-15 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
- 5 80. A composition comprising: a 15-20 amino peptide means for activating a delta opioid receptor, and a pharmaceutically acceptable carrier or excipient.
81. A composition comprising: a 15-20 amino peptide means for inducing analgesia in a living subject, and a pharmaceutically acceptable carrier or excipient.
82. A method of activating a delta opioid receptor, the method comprising contacting a delta
10 opioid receptor, or a cell comprising a delta opioid receptor, with a composition according to any one of claims 50-81.
83. A method of activating a delta opioid receptor in a living subject in need thereof, the method comprising administering to the subject a composition according to any one of claims 50-81.
- 15 84. A method of inducing analgesia in a subject in need thereof, the method comprising administering to the subject an effective amount of a composition according to any one of claims 50-81.