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PEPTIDES AND METHODS OF USE THEREOF IN TREATING SKIN DISEASES

Abstract

The present disclosure includes methods of treating a disease or condition that produces skin inflammation and/or itch. More specifically the present disclosure relates to treating skin inflammation and itch caused by diseases or disorders of the skin such as psoriasis by administering a peptide fragment of the MARCKS protein. Peptide fragments and variants thereof as disclosed in the present disclosure are useful in such methods.

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Background/Summary

CROSS REFERENCE TO RELATED APPLICATIONS [0001] This application claims priority from U.S. Provisional Application No. 63/334,366 filed Apr. 25, 2022, which is incorporated by reference herein in its entirety for all purposes.

TECHNICAL FIELD
[0003] The present disclosure relates to peptides or peptide compositions or peptide formulations and methods of their use to treat skin diseases or disorders such as psoriasis or atopic dermatitis. The present disclosure also relates to topical formulations of such peptides.
DESCRIPTION OF THE TEXT FILE SUBMITTED ELECTRONICALLY
[0004] The Sequence Listing XML associated with this application is provided in XML file format and is herein incorporated by reference into the specification. The name of the XML file containing the Sequence Listing XML is BMRK_009_01WO_SeqList_ST26.xml. The XML file is 418,416 bytes, was created on Feb. 24, 2023, and is being submitted electronically via U.S. Patent Center.
BACKGROUND
[0005] Atopic dermatitis (AD) is a chronic illness of both children and adults and is often a lifelong disease worldwide. AD poses the second-highest disability rank of all non-malignant skin diseases and is characterized by relapsing skin inflammation and itch. Another disease with similar symptoms (e.g., skin inflammation and itch) to AD is psoriasis. Numerous immune and non-immune cells have been implicated in the pathogenesis of AD and psoriasis including mast cell, neutrophils, basophils and T helper type 2 (Th2) cells. Additionally, keratinocytes have been shown to be critical contributors to the development of AD and itch, whereby skin keratinocytes are activated by cytokine thymic stromal lymphopoietin (TSLP) by both autocrine or paracrine mechanisms and serve as a rapid source of periostin and TSLP that drive AD pathogenesis including inflammation and itch behavior (Mishra S K et al., Cell Reports, 2020).
[0006] Emerging evidence from studies suggests that myristoylated alanine-rich C kinase substrate (MARCKS) protein regulates pro-inflammatory NF-kB in macrophages. While MARCKS protein has been shown to be expressed by keratinocytes, who play a key role in providing a first line of defense for an individual by constituting a solid physical skin barrier, the role of said MARCKS protein expression in said keratinocytes currently remains unknown. Thus, there is an urgent need to correct this knowledge gap to develop novel therapies for AD and psoriasis.
SUMMARY
[0007] The disclosure provides a method of treating a skin disease, skin disorder or skin condition or one or more symptoms associated with a skin disorder, skin disease or skin condition in a subject comprising, administering to said subject a therapeutically effective amount of a composition comprising at least one peptide having an amino acid sequence selected from the group consisting of: (a) an amino acid sequence having from 4 to 24 contiguous amino acids of a reference sequence, GAQFSKTAAKGEAAAERPGEAAVA (SEQ ID NO. 1); (b) an amino acid sequence having the sequence, GAQFSKTAAKGEAAAERPGEAAVA (SEQ ID NO. 1); and (c) an amino acid sequence with at least about 75% identity to the amino acid sequence defined in (a) or (b). In

some cases, the skin disease, skin disorder or skin condition is psoriasis. In some cases, the skin disease, skin disorder or skin condition is an autoinflammatory skin disease such as a neutrophilic dermatoses. In some cases, the autoinflammatory skin disease is pyoderma gangrenosum. In some cases, the one or more symptoms associated with the skin disease, skin disorder or skin condition is selected from the group consisting of skin thickness, skin dryness, skin flakiness, skin bumps, skin nodules, skin pustules, skin redness, skin ulceration and any combination thereof.

[0008] In some aspects, the peptide comprises at least four, at least five, at least six, at least seven, at least eight, at least nine or at least ten contiguous amino acid residues of SEQ ID NO: 1. In some aspects, the peptide comprises at least ten contiguous amino acid residues of SEQ ID NO: 1. In some aspects, the peptide comprises an amino acid sequence of SEQ ID NO: 106. In some aspects, the peptide consists of at least four contiguous amino acid residues of SEQ ID NO: 1. In some cases, the peptide comprises an amino acid sequence of SEQ ID NO: 219. In some aspects, the peptide is myristoylated or acetylated at the N-terminal amino acid. In some aspects, the peptide is acetylated at the N-terminal amino acid and consists of an amino acid sequence of SEQ ID NO: 106 or 219. In some aspects, the peptide is acetylated at the N-terminal amino acid and consists of an amino acid sequence of SEQ ID NO: 106. In some aspects, the peptide is acetylated at the N-terminal amino acid and consists of an amino acid sequence of SEQ ID NO: 219. In some cases, the peptide is BIO-11006 (Ac-GAQFSKTAAK-OH). In some cases, the peptide is BIO-91201 (Ac-AKGE-OH). In some cases, the peptide is BIO-91202 (Ac-AKGE-NH2).

[0009] In some aspects, the composition comprises a pharmaceutically acceptable carrier. In some aspects, the subject is a mammal. In some aspects, the mammal is selected from the group consisting of humans, canines, rodents, equines and felines.

[0010] In some aspects, the composition comprises a topical administration, intravenous injection, intraperitoneal (ip) administration or any combination thereof. In some aspects, the administering is done by intraperitoneal administration. In some aspects, the present disclosure provides intraperitoneal formulations comprising one or more of the peptides disclosed herein. In some embodiments, the composition is administered by daily administrations. In some embodiments, each daily topical administration comprises one, two, three, four, or five administrations on each day, for example, approximately one administration every 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 hours. In some embodiments, on each day that the composition is administered intraperitoneally, the composition is administered once, twice, or three times.

[0011] In some aspects, the method further comprises administration to the subject a second molecule, wherein the second molecule is an antibiotic, an antiviral compound, an antiparasitic compound, an antifungal compound, an antihistamine compound, an anti-inflammatory compound, an immunomodulatory compound, corticosteroid, an immunosuppressant or any combination thereof.

Description

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIG. **1**A illustrates the methodological details of an MC903 induced mouse model of atopic dermatitis (AD). In particular, shown is a timeline of the AD induction model and application of the MARCKS inhibitor (BIO 11006) and the three different outcomes analyzed.

[0013] FIG. **1**B illustrates the skin thickness in micrometers of mice administered MC903 daily for ten (10) days in order to mimic atopic dermatitis (AD) in each of four (4) test groups as compared to the skin thickness in micrometers of mice from either of two (2) control groups. The four (4) test groups consisted of mice administered MC903 daily plus intraperitoneal (ip) injection of BIO 11006 as either (1) a single dose on day 10, (2) a single dose on each of days 9 and 10, (3) a single dose on each of days 4-10, and (4) a daily single dose on each of days 1-10. The two (2) control

groups consisted of (1) mice administered the vehicle only and (2) mice administered MC903 daily and vehicle only.

[0014] FIG. **2**A illustrates the methodological details of an imiquimod induced mouse model of psoriasis. In particular, shown is a timeline of the psoriasis induction model and application of the MARCKS inhibitor (BIO 11006) and the three different outcomes analyzed.

[0015] FIG. **2**B illustrates the skin thickness in micrometers of mice administered imiquimod daily for seven (7) days in order to mimic psoriasis in one (1) test group as compared to the skin thickness in micrometers from either of two (2) control groups. The test group consisted of mice administered imiquimod daily plus intraperitoneal (ip) injection of BIO 11006 as a daily single dose on each of days 1-7. The two (2) control groups consisted of (1) mice administered vaseline and (2) mice administered imiquimod daily and phosphate buffered saline (PBS). N=6-7 mice, mean+SD, 1-way ANOVA, Tukey test.

[0016] FIG. **3** depicts images of mice the skin on the nape of the neck for the test group and two control groups described for FIG. **2**B and Example 1. #1, 2 and 3 represent same treatments.

[0017] FIG. **4** illustrates the percent dryness, flakiness, skin bumps and redness the skin on the nape of the neck for the test group and two control groups described for FIG. **2**B and Example 1. At a scale of 0-5, 0 indicated no visible signs or symptoms; 1-3 indicated moderate forms of the respective sign or symptom; 4-5 indicated major forms of the respective sign or symptom.

DETAILED DESCRIPTION

Definitions

[0018] It is to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting.

[0019] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood to one of ordinary skill in the art to which the present application belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present application, representative methods and materials are herein described.

[0020] Following long-standing patent law convention, the terms “a”, “an”, and “the” refer to “one or more” when used in this application, including the claims. Thus, for example, reference to “a carrier” includes mixtures of one or more carriers, two or more carriers, and the like and reference to “the method” includes reference to equivalent steps and/or methods known to those skilled in the art, and so forth.

[0021] Unless otherwise indicated, all numbers expressing quantities of ingredients, reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term “about”. Accordingly, unless indicated to the contrary, the numerical parameters set forth in the present specification and attached claims are approximations that can vary depending upon the desired properties sought to be obtained by the present application. Generally, the term “about”, as used herein in references to a measurable value such as an amount of weight, time, dose, etc. is meant to encompass values within an acceptable degree of variability in the art. In some embodiments, degree of variability is based on FDA guidelines.

[0022] As used herein, “treating” or “treatment” and the like is an approach for obtaining beneficial or desired clinical results. For purposes of this disclosure, beneficial or desired clinical results include, but are not limited to, one or more of the following: alleviation of one or more symptoms of an ocular condition at the surface of the eye such as dry eye syndrome. Symptoms of such an ocular condition include, but are not limited to, pain or discomfort in the eye, dryness in the eye, itchiness in the eye, a burning, stinging, or irritating feeling in the eye or a feeling that a foreign object is in the eye, and sensitivity to light. Accordingly, the terms “treating” or “treatment” and the like include lessening the severity of such symptoms in the eye, including reducing the incidence of, managing, ameliorating, preventing, and/or delaying the development or progression of such symptoms in the eye. Treating or treatment herein can also include improving vision or preventing,

stopping, or slowing the progression of vision loss.

[0023] The term “effective amount” or “therapeutically effective amount” refers to the amount of an agent that is sufficient to achieve an outcome, for example, to affect beneficial or desired results. The therapeutically effective amount may vary depending upon one or more of: the subject and disease condition being treated, the weight and age of the subject, the severity of the disease condition, the manner of administration and the like.

MARCKS Protein

[0024] MARCKS protein is an actin-binding protein and contributes to cytoskeleton orientation and function, and cell migration. Several exogenous stimuli can provoke degranulation of leukocytes via a pathway that involves activation of protein kinase C and subsequent phosphorylation and dephosphorylation events. MARCKS protein (where MARCKS as used herein means “Myristoylated Alanine-Rich C Kinase Substrate”), is a ubiquitous phosphorylation target of protein kinase C (PKC) and is highly expressed in leukocytes. MARCKS protein is mechanistically involved in a process of exocytotic secretion of mucin by goblet cells that line respiratory airways. MARCKS, a protein of approximately 82 kD, has three evolutionarily-conserved regions, an N-terminus, a phosphorylation site domain (or PSD), and a multiple homology 2 (MH2) domain. MARCKS is myristoylated via an amide bond at the N-terminal amino acid in the MARCKS protein's amino acid sequence at the alpha-amine position of the glycine which resides at the N-terminus (i.e., at position 1) of amino acid sequence via a reaction catalyzed by myristoyl CoA:protein N-myristoyl transferase (NMT). The mechanism appears to involve binding of MARCKS, a myristoylated protein, to membranes of intracellular granules.

[0025] The myristoylated N-terminal region of MARCKS appears to be integral to the secretory process because it has been shown to block both mucin secretion and binding of MARCKS to mucin granule membranes in goblet cells. This peptide contains 24 L-amino acids of the MARCKS protein beginning with the N-terminal glycine of the MARCKS protein which is myristoylated via an amide bond and is known as myristoylated alpha-N-terminal sequence (or “MANS”, also interchangeably referred to as the “MARCKS N-terminus”); i.e., Myristoyl-GAQFSKTAAKGEAAAERPGEAAVA (SEQ ID NO: 1). The peptide fragments of the MANS peptide disclosed herein, also preferably are composed of L-amino acids. As MARCKS is an actin-binding protein, it is critical for cytoskeleton orientation and function and cell migration. In some embodiments, the N-terminal MARCKS peptides disclosed herein inhibit directed migration of human neutrophils, fibroblasts, and airway epithelial cells.

Peptides Derived from N-Terminus of MARCKS

[0026] The disclosure provides peptides fragments (interchangeably referred to as just “fragments” or just “peptides”) derived from the MARCKS N-terminus. Exemplary MARCKS-related peptide fragments are discussed in U.S. Publication Nos. 2009-0203620 and 2014-0302057, and in International Patent Publication No. WO 2020/257162, the entire contents of each of which are incorporated herein by reference. In some aspects, these peptide fragments play a role in the reducing the rate and/or amount of release of inflammatory mediators, granules or vesicles in inflammatory leukocytes.

[0027] In some aspects, the peptides disclosed herein are derived from the MARCKS N-terminus, i.e., contiguous peptide fragments derived from within the N-terminal 1-to-24 amino acid sequence of MARCKS. In some aspects, the peptides are N-terminal amides of such fragments, such as N-terminal acetic acid amides of such fragments, and/or as well as C-terminal amides of such fragments, such as C-terminal amides of ammonia. In some aspects, the peptides have from about 4 to about 23 contiguous amino acid residues of the MANS peptide amino acid sequence. In some aspects, the fragments may be N-terminal-myristoylated if they do not begin with the N-terminal glycine at position 1 in SEQ ID NO: 1 or may be N-terminal-acylated with C2 to C12 acyl groups, including N-terminal-acetylated, and/or C-terminal amidated with an NH2 group.

[0028] Table 1 contains a list of amino acid sequences in single letter abbreviation format together

with a respectively corresponding peptide number and SEQ ID NO. The reference peptide amino acid sequence (MANS peptide) is listed as peptide 1. Amino acid sequences of peptides of the disclosure having an amino acid sequence of from 4 to 23 contiguous amino acids of the reference amino acid sequence are listed as peptides 2 to 231, together with the amino acid sequence of a random N-terminal sequence (RNS) comprising amino acids of the MANS peptide as peptide 232. Amino acid sequences of representative variants of amino acid sequences of peptides of the disclosure as described herein and are also listed as peptides 233 to 245 and 247 to 251. The variant peptides listed are not intended to be a limiting group of peptides but are presented only to serve as representative examples of variant peptides of the disclosure. Also presented is a representative reverse amino acid sequence (peptide 246) and a representative random amino acid sequence of peptide (peptide 232) of the disclosure.

[0029] In some aspects, the peptide comprises an amino acid sequence with at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, or at least about 99.5% identity to any one of the amino acid sequences listed in Table 1. In some aspects, the peptide comprises any one of the amino acid sequences listed in Table 1. In some aspects, the peptides consist of any one of the amino acid sequences listed in Table 1.

TABLE-US-00001 TABLE 1 Peptides and Amino Acid Sequences Peptide No. Sequence Sequence ID No. peptide 1 GAQFSKTAAKGEAAAERPGEAAVA SEQ ID NO. 1 peptide 2 GAQFSKTAAKGEAAAERPGEAAV SEQ ID NO. 2 peptide 3 AQFSKTAAKGEAAAERPGEAAVA SEQ ID NO. 3 peptide 4 GAQFSKTAAKGEAAAERPGEAA SEQ ID NO. 4 peptide 5 AQFSKTAAKGEAAAERPGEAAV SEQ ID NO. 5 peptide 6 QFSKTAAKGEAAAERPGEAAVA SEQ ID NO. 6 peptide 7 GAQFSKTAAKGEAAAERPGEA SEQ ID NO. 7 peptide 8 AQFSKTAAKGEAAAERPGEAA SEQ ID NO. 8 peptide 9 QFSKTAAKGEAAAERPGEAAV SEQ ID NO. 9 peptide 10 FSKTAAKGEAAAERPGEAAVA SEQ ID NO. 10 peptide 11 GAQFSKTAAKGEAAAERPGE SEQ ID NO. 11 peptide 12 AQFSKTAAKGEAAAERPGEA SEQ ID NO. 12 peptide 13 QFSKTAAKGEAAAERPGEAA SEQ ID NO. 13 peptide 14 FSKTAAKGEAAAERPGEAAV SEQ ID NO. 14 peptide 15 SKTAAKGEAAAERPGEAAVA SEQ ID NO. 15 peptide 16 GAQFSKTAAKGEAAAERPG SEQ ID NO. 16 peptide 17 AQFSKTAAKGEAAAERPGE SEQ ID NO. 17 peptide 18 QFSKTAAKGEAAAERPGEA SEQ ID NO. 18 peptide 19 FSKTAAKGEAAAERPGEAA SEQ ID NO. 19 peptide 20 SKTAAKGEAAAERPGEAAV SEQ ID NO. 20 peptide 21 KTAAKGEAAAERPGEAAVA SEQ ID NO. 21 peptide 22 GAQFSKTAAKGEAAAERP SEQ ID NO. 22 peptide 23 AQFSKTAAKGEAAAERPG SEQ ID NO. 23 peptide 24 QFSKTAAKGEAAAERPGE SEQ ID NO. 24 peptide 25 FSKTAAKGEAAAERPGEA SEQ ID NO. 25 peptide 26 SKTAAKGEAAAERPGEAA SEQ ID NO. 26 peptide 27 KTAAKGEAAAERPGEAAV SEQ ID NO. 27 peptide 28 TAAKGEAAAERPGEAAVA SEQ ID NO. 28 peptide 29 GAQFSKTAAKGEAAAER SEQ ID NO. 29 peptide 30 AQFSKTAAKGEAAAERP SEQ ID NO. 30 peptide 31 QFSKTAAKGEAAAERPG SEQ ID NO. 31 peptide 32 FSKTAAKGEAAAERPGE SEQ ID NO. 32 peptide 33 SKTAAKGEAAAERPGEA SEQ ID NO. 33 peptide 34 KTAAKGEAAAERPGEAA SEQ ID NO. 34 peptide 35 TAAKGEAAAERPGEAAV SEQ ID NO. 35 peptide 36 AAKGEAAAERPGEAAVA SEQ ID NO. 36 peptide 37 GAQFSKTAAKGEAAAE SEQ ID NO. 37 peptide 38 AQFSKTAAKGEAAAER SEQ ID NO. 38 peptide 39 QFSKTAAKGEAAAERP SEQ ID NO. 39 peptide 40 FSKTAAKGEAAAERPG SEQ ID NO. 40 peptide 41

SKTAAKGEAAAERPGE SEQ ID NO. 41 peptide 42 KTAAKGEAAAERPGEA SEQ ID NO. 42 peptide 43 TAAKGEAAAERPGEAA SEQ ID NO. 43 peptide 44 AAKGEAAAERPGEAAV SEQ ID NO. 44 peptide 45 AKGEAAAERPGEAAVA SEQ ID NO. 45 peptide 46 GAQFSKTAAKGEAAA SEQ ID NO. 46 peptide 47 AQFSKTAAKGEAAAE SEQ ID NO. 47 peptide 48 QFSKTAAKGEAAAER SEQ ID NO. 48 peptide 49 FSKTAAKGEAAAERP SEQ ID NO. 49 peptide 50 SKTAAKGEAAAERPG SEQ ID NO. 50 peptide 51 KTAAKGEAAAERPGE SEQ ID NO. 51 peptide 52 TAAKGEAAAERPGEA SEQ ID NO. 52 peptide 53 AAKGEAAAERPGEAA SEQ ID NO. 53 peptide 54 AKGEAAAERPGEAAV SEQ ID NO. 54 peptide 55 KGEAAAERPGEAAVA SEQ ID NO. 55 peptide 56 GAQFSKTAAKGEAA SEQ ID NO. 56 peptide 57 AQFSKTAAKGEAAA SEQ ID NO. 57 peptide 58 QFSKTAAKGEAAAE SEQ ID NO. 58 peptide 59 FSKTAAKGEAAAER SEQ ID NO. 59 peptide 60 SKTAAKGEAAAERP SEQ ID NO. 60 peptide 61 KTAAKGEAAAERPG SEQ ID NO. 61 peptide 62 TAAKGEAAAERPGE SEQ ID NO. 62 peptide 63 AAKGEAAAERPGEA SEQ ID NO. 63 peptide 64 AKGEAAAERPGEAA SEQ ID NO. 64 peptide 65 KGEAAAERPGEAAV SEQ ID NO. 65 peptide 66 GEAAAERPGEAAVA SEQ ID NO. 66 peptide 67 GAQFSKTAAKGEA SEQ ID NO. 67 peptide 68 AQFSKTAAKGEAA SEQ ID NO. 68 peptide 69 QFSKTAAKGEAAA SEQ ID NO. 69 peptide 70 FSKTAAKGEAAAE SEQ ID NO. 70 peptide 71 SKTAAKGEAAAER SEQ ID NO. 71 peptide 72 KTAAKGEAAAERP SEQ ID NO. 72 peptide 73 TAAKGEAAAERPG SEQ ID NO. 73 peptide 74 AAKGEAAAERPGE SEQ ID NO. 74 peptide 75 AKGEAAAERPGEA SEQ ID NO. 75 peptide 76 KGEAAAERPGEAA SEQ ID NO. 76 peptide 77 GEAAAERPGEAAV SEQ ID NO. 77 peptide 78 EAAAERPGEAAVA SEQ ID NO. 78 peptide 79 GAQFSKTAAKGE SEQ ID NO. 79 peptide 80 AQFSKTAAKGEA SEQ ID NO. 80 peptide 81 QFSKTAAKGEAA SEQ ID NO. 81 peptide 82 FSKTAAKGEAAA SEQ ID NO. 82 peptide 83 SKTAAKGEAAAE SEQ ID NO. 83 peptide 84 KTAAKGEAAAER SEQ ID NO. 84 peptide 85 TAAKGEAAAERP SEQ ID NO. 85 peptide 86 AAKGEAAAERPG SEQ ID NO. 86 peptide 87 AKGEAAAERPGE SEQ ID NO. 87 peptide 88 KGEAAAERPGEA SEQ ID NO. 88 peptide 89 GEAAAERPGEAA SEQ ID NO. 89 peptide 90 EAAAERPGEAAV SEQ ID NO. 90 peptide 91 AAAERPGEAAVA SEQ ID NO. 91 peptide 92 GAQFSKTAAKG SEQ ID NO. 92 peptide 93 AQFSKTAAKGE SEQ ID NO. 93 peptide 94 QFSKTAAKGEA SEQ ID NO. 94 peptide 95 FSKTAAKGEAA SEQ ID NO. 95 peptide 96 SKTAAKGEAAA SEQ ID NO. 96 peptide 97 KTAAKGEAAAE SEQ ID NO. 97 peptide 98 TAAKGEAAAER SEQ ID NO. 98 peptide 99 AAKGEAAAERP SEQ ID NO. 99 peptide 100 AKGEAAAERPG SEQ ID NO. 100 peptide 101 KGEAAAERPGE SEQ ID NO. 101 peptide 102 GEAAAERPGEA SEQ ID NO. 102 peptide 103 EAAAERPGEAA SEQ ID NO. 103 peptide 104 AAAERPGEAAV SEQ ID NO. 104 peptide 105 AAERPGEAAVA SEQ ID NO. 105 peptide 106 GAQFSKTAAK SEQ ID NO. 106 peptide 107 AQFSKTAAKG SEQ ID NO. 107 peptide 108 QFSKTAAKGE SEQ ID NO. 108 peptide 109 FSKTAAKGEA SEQ ID NO. 109 peptide 110 SKTAAKGEAA SEQ ID NO. 110 peptide 111 KTAAKGEAAA SEQ ID NO. 111 peptide 112 TAAKGEAAAE SEQ ID NO. 112 peptide 113 AAKGEAAAER SEQ ID NO. 113 peptide 114 AKGEAAAERP SEQ ID NO. 114 peptide 115 KGEAAAERPG SEQ ID NO. 115 peptide 116 GEAAAERPGE SEQ ID NO. 116 peptide 117 EAAAERPGEA SEQ ID NO. 117 peptide 118 AAAERPGEAA SEQ ID NO. 118 peptide 119 AAERPGEAAV SEQ ID NO. 119 peptide 120 AERPGEAAVA SEQ ID NO. 120 peptide 121 GAQFSKTAA SEQ ID NO. 121 peptide 122 AQFSKTAAK SEQ ID

NO. 122 peptide 123 QFSKTAAKG SEQ ID NO. 123 peptide 124 FSKTAAKGE SEQ ID NO. 124 peptide 125 SKTAAKGEA SEQ ID NO. 125 peptide 126 KTAAKGEAA SEQ ID NO. 126 peptide 127 TAAKGEAAA SEQ ID NO. 127 peptide 128 AAKGEAAAE SEQ ID NO. 128 peptide 129 AKGEAAAER SEQ ID NO. 129 peptide 130 KGEAAAERP SEQ ID NO. 130 peptide 131 GEAAAERPG SEQ ID NO. 131 peptide 132 EAAAERPGE SEQ ID NO. 132 peptide 133 AAAERPGEA SEQ ID NO. 133 peptide 134 AAERPGEAA SEQ ID NO. 134 peptide 135 AERPGEAAV SEQ ID NO. 135 peptide 136 ERPGEAAVA SEQ ID NO. 136 peptide 137 GAQFSKTA SEQ ID NO. 137 peptide 138 AQFSKTAA SEQ ID NO. 138 peptide 139 QFSKTAAK SEQ ID NO. 139 peptide 140 FSKTAAKG SEQ ID NO. 140 peptide 141 SKTAAKGE SEQ ID NO. 141 peptide 142 KTAAKGEA SEQ ID NO. 142 peptide 143 TAAKGEAA SEQ ID NO. 143 peptide 144 AAKGEAAA SEQ ID NO. 144 peptide 145 AKGEAAAE SEQ ID NO. 145 peptide 146 KGEAAAER SEQ ID NO. 146 peptide 147 GEAAAERP SEQ ID NO. 147 peptide 148 EAAAERPG SEQ ID NO. 148 peptide 149 AAAERPGE SEQ ID NO. 149 peptide 150 AAERPGEA SEQ ID NO. 150 peptide 151 AERPGEAA SEQ ID NO. 151 peptide 152 ERPGEAAV SEQ ID NO. 152 peptide 153 RPGEAAVA SEQ ID NO. 153 peptide 154 GAQFSKT SEQ ID NO. 154 peptide 155 AQFSKTA SEQ ID NO. 155 peptide 156 QFSKTAA SEQ ID NO. 156 peptide 157 FSKTAAK SEQ ID NO. 157 peptide 158 SKTAAKG SEQ ID NO. 158 peptide 159 KTAAKGE SEQ ID NO. 159 peptide 160 TAAKGEA SEQ ID NO. 160 peptide 161 AAKGEAA SEQ ID NO. 161 peptide 162 AKGEAAA SEQ ID NO. 162 peptide 163 KGEAAAE SEQ ID NO. 163 peptide 164 GEAAAER SEQ ID NO. 164 peptide 165 EAAAERP SEQ ID NO. 165 peptide 166 AAAERPG SEQ ID NO. 166 peptide 167 AAERPGE SEQ ID NO. 167 peptide 168 AERPGEA SEQ ID NO. 168 peptide 169 ERPGEAA SEQ ID NO. 169 peptide 170 RPGEAAV SEQ ID NO. 170 peptide 171 PGEAAVA SEQ ID NO. 171 peptide 172 GAQFSK SEQ ID NO. 172 peptide 173 AQFSKT SEQ ID NO. 173 peptide 174 QFSKTA SEQ ID NO. 174 peptide 175 FSKTAA SEQ ID NO. 175 peptide 176 SKTAAK SEQ ID NO. 176 peptide 177 KTAAKG SEQ ID NO. 177 peptide 178 TAAKGE SEQ ID NO. 178 peptide 179 AAKGEA SEQ ID NO. 179 peptide 180 AKGEAA SEQ ID NO. 180 peptide 181 KGEAAA SEQ ID NO. 181 peptide 182 GEAAAE SEQ ID NO. 182 peptide 183 EAAAER SEQ ID NO. 183 peptide 184 AAAERP SEQ ID NO. 184 peptide 185 AAERPG SEQ ID NO. 185 peptide 186 AERPGE SEQ ID NO. 186 peptide 187 ERPGEA SEQ ID NO. 187 peptide 188 RPGEAA SEQ ID NO. 188 peptide 189 PGEAAV SEQ ID NO. 189 peptide 190 GEAAVA SEQ ID NO. 190 peptide 191 GAQFS SEQ ID NO. 191 peptide 192 AQFSK SEQ ID NO. 192 peptide 193 QFSKT SEQ ID NO. 193 peptide 194 FSKTA SEQ ID NO. 194 peptide 195 SKTAA SEQ ID NO. 195 peptide 196 KTAAK SEQ ID NO. 196 peptide 197 TAAKG SEQ ID NO. 197 peptide 198 AAKGE SEQ ID NO. 198 peptide 199 AKGEA SEQ ID NO. 199 peptide 200 KGEAA SEQ ID NO. 200 peptide 201 GEAAA SEQ ID NO. 201 peptide 202 EAAAE SEQ ID NO. 202 peptide 203 AAAER SEQ ID NO. 203 peptide 204 AAERP SEQ ID NO. 204 peptide 205 AERPG SEQ ID NO. 205 peptide 206 ERPGE SEQ ID NO. 206 peptide 207 RPGEA SEQ ID NO. 207 peptide 208 PGEAA SEQ ID NO. 208 peptide 209 GEAAV SEQ ID NO. 209 peptide 210 EAAVA SEQ ID NO. 210 peptide 211 GAQF SEQ ID NO. 211 peptide 212 AQFS SEQ ID NO. 212 peptide 213 QFSK SEQ ID NO. 213 peptide 214 FSKT SEQ ID NO. 214 peptide 215 SKTA SEQ ID NO. 215 peptide 216 KTAA SEQ ID NO. 216 peptide 217 TAAK SEQ ID NO. 217 peptide 218 AAKG SEQ ID NO. 218 peptide 219 AKGE SEQ ID NO. 219

peptide 220 KGEA SEQ ID NO. 220 peptide 221 GEAA SEQ ID NO. 221 peptide 222 EAAA SEQ ID NO. 222 peptide 223 AAAE SEQ ID NO. 223 peptide 224 AAER SEQ ID NO. 224 peptide 225 AERP SEQ ID NO. 225 peptide 226 ERPG SEQ ID NO. 226 peptide 227 RPGE SEQ ID NO. 227 peptide 228 PGEA SEQ ID NO. 228 peptide 229 GEAA SEQ ID NO. 229 peptide 230 EAAV SEQ ID NO. 230 peptide 231 AAVA SEQ ID NO. 231 peptide 232 GTAPAAEGAGAEVKRASAEAKQAF SEQ ID NO. 232 peptide 233 GKQFSKTAAKGE SEQ ID NO. 233 peptide 234 GAQFSKTKAKGE SEQ ID NO. 234 peptide 235 GKQFSKTKAKGE SEQ ID NO. 235 peptide 236 GAQASKTAAK SEQ ID NO. 236 peptide 237 GAQASKTAAKGE SEQ ID NO. 237 peptide 238 GAEFSKTAAKGE SEQ ID NO. 238 peptide 239 GAQFSKTAAAGE SEQ ID NO. 239 peptide 240 GAQFSKTAAKAE SEQ ID NO. 240 peptide 241 GAQFSKTAAKGA SEQ ID NO. 241 peptide 242 AAQFSKTAAK SEQ ID NO. 242 peptide 243 GAAFSKTAAK SEQ ID NO. 243 peptide 244 GAQFAKTAAK SEQ ID NO. 244 peptide 245 GAQFSATAAK SEQ ID NO. 245 peptide 246 KAATKSFQAG SEQ ID NO. 246 peptide 247 GAQFSKAAAK SEQ ID NO. 247 peptide 248 GAQFSKTAAA SEQ ID NO. 248 peptide 249 GAQFSATAAA SEQ ID NO. 249 peptide 250 GAQASKTA SEQ ID NO. 250 peptide 251 AAGE SEQ ID NO. 251 peptide 252 GKASQFAKTA SEQ ID NO. 252

[0030] In some aspects, the peptide is any one of the peptides listed in Table 1A.

TABLE-US-00002 TABLE 1A Peptide Name Seq ID NO. MANS 1 Ac-MANS 1 BIO-11211 (Ac—NH2) 79 BIO-11000 (Ma—OH) 106 BIO-11002 (Ma—NH2) 106 BIO-11005 (H—NH2 106 BIO-11006 (Ac—OH) 106 BIO-11007 (cyclic) 106 cyclic BIO-11018 (pegylated) 106 pegylated BIO-11026 (Ac—NH2) 106 BIO-10901 (Ac—OH) 121 BIO-10803 (Ac—OH) 137 BIO-91200 (Ma-AKGE-OH) 219 BIO-91201 (Ac-AKGE-OH) 219 BIO-91202 (Ac-AKGE-NH2) 219 Ma = Myristoyl; Ac = Acetyl

[0031] The disclosure provides peptides having amino acid sequences comprising less than 24 amino acids with amino acid sequences related to the amino acid sequence of MANS peptide. The peptides of the current disclosure consist of amino acid sequences containing less than 24 amino acids, and may consist of from 4 to 14, from 10 to 12, from 9 to 14, from 9 to 13, from 10 to 13, from 10 to 14, at least 4, at least 9, at least 10, or the like amino acids. The peptides are typically straight chains but may be cyclic peptides as well. Cyclic peptides are peptides that contain a circular or cyclic ring structure. The circular ring structure can be formed, for example, through connection between the amino and carboxyl ends of the peptide, or between the carboxyl or amino end and a side chain, or between a peptide backbone and the carboxyl or amino end or a side chain, or between two positions on the peptide backbone, or between two side chains. The connections may be formed via an amide bond, or other chemically stable bonds. In some embodiments, the peptide is a head-to-tail cyclic peptide. In some embodiments, the peptides are pegylated (PEGylated). PEGylating is the process of covalently attaching polyethylene glycol (PEG) chains to peptides. In some embodiments, PEGylating enhances solubility and/or half-life of peptides, and/or reduces immunogenicity. Thus, in some embodiments, peptide PEGylation therapeutic efficacy and/or tolerability of peptide drugs. In some embodiments, the peptides are synthetic peptides. In some embodiments, the peptides are isolated peptides.

[0032] In some aspects, the peptide has an amino acid sequence selected from the group consisting of (a) an amino acid sequence having from 4 to 23 contiguous amino acids of the reference sequence, peptide 1; (b) a sequence with at least about 75%, at least about 80% identity, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, or at least about 95% identity to the amino acid sequence defined in (a); or (c) a variant of the amino acid sequence defined in (a), which variant is selected from the group consisting of a substitution variant, a deletion variant, an addition variant, and combinations thereof.

[0033] In other embodiments, the amino acid sequence of the peptide does not begin at the N-terminal amino acid of the reference sequence, peptide 1, (SEQ ID NO: 1) but rather begins at the amino acid at position 2 through the amino acid at position 21 of the reference sequence peptide 1. For example, the peptides may have an amino acid sequence selected from the group consisting of (a) an amino acid sequence having from 4 to 23 contiguous amino acids of the reference sequence peptide 1, wherein the amino acid sequence begins at any amino acid between position 2 through position 21 of the reference sequence. These peptides may be between 4 and 23 contiguous amino acids long and may represent peptides in the middle of the reference sequence, peptide 1; (b) a sequence with at least about 75%, at least 80% about identity, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, or at least about 95% identity to the amino acid sequence defined in (a); or (c) a variant of the amino acid sequence defined in (a). These peptides may contain no covalently bound chemical moiety or a chemical moiety on the N-terminal amino acid which is not the N-terminal glycine from or equivalent to the N-terminal glycine of the amino acid sequence SEQ ID NO: 1. Preferably, the chemical moiety is an acyl group, such as an acetyl group or a myristoyl group, in the form of an amide bond, or an alkyl group.

[0034] Peptide amino acid sequences which are useful in the current invention to treat, prevent or ameliorate skin inflammation and/or itch, and/or which are useful to treat skin disease(s), disorder(s) or condition(s) in a mammal include amino acid sequences of isolated peptides and amino acid sequences of peptides which optionally contain N-terminal- and/or C-terminal-chemically modified groups of the current invention, which peptide amino acid sequences are selected from the group consisting of the 23-mers (i.e., peptides having a 23 amino acid sequence): PEPTIDE 2; and PEPTIDE 3; the 22-mers (i.e., peptides having a 22 amino acid sequence): PEPTIDE 4; PEPTIDE 5; and PEPTIDE 6; the 21-mers (i.e., peptides having a 21 amino acid sequence): PEPTIDE 7; PEPTIDE 8; PEPTIDE 9; and PEPTIDE 10; the 20-mers (i.e., peptides having a 20 amino acid sequence): PEPTIDE 11; PEPTIDE 12; PEPTIDE 13; PEPTIDE 14; and PEPTIDE 15; the 19-mers (i.e., peptides having a 19 amino acid sequence): PEPTIDE 16; PEPTIDE 17; PEPTIDE 18; PEPTIDE 19; PEPTIDE 20; and PEPTIDE 21; the 18-mers (i.e., peptides having a 18 amino acid sequence): PEPTIDE 22; PEPTIDE 23; peptide 25; peptide 26; peptide 27; and peptide 28; the 17-mers (i.e., peptides having a 17 amino acid sequence): peptide 29; peptide 30; peptide 31; peptide 32; peptide 33; peptide 34; peptide 35; and peptide 36; the 16-mers (i.e., peptides having a 16 amino acid sequence): peptide 37; peptide 38; peptide 39; peptide 40; peptide 41; peptide 42; peptide 43; peptide 44; and peptide 45; the 15-mers (i.e., peptides having a 15 amino acid sequence): peptide 46; peptide 47; peptide 48; peptide 49; peptide 50; peptide 51; peptide 52; peptide 53; peptide 54; and peptide 55; the 14-mers (i.e., peptides having a 14 amino acid sequence): peptide 56; peptide 57; peptide 58; peptide 59; peptide 60; peptide 61; peptide 62; peptide 63; peptide 64; peptide 65; and peptide 66; the 13-mers (i.e., peptides having a 13 amino acid sequence): peptide 67; peptide 68; peptide 69; peptide 70; peptide 71; peptide 72; peptide 73; peptide 74; peptide 75; peptide 76; peptide 77; and peptide 78; the 12-mers (i.e., peptides having a 12 amino acid sequence): peptide 79; peptide 80; peptide 81; peptide 82; peptide 83; peptide 84; peptide 85; peptide 86; peptide 87; peptide 88; peptide 89; peptide 90; and peptide 91; the 11-mers (i.e., peptides having a 11 amino acid sequence): peptide 92; peptide 93; peptide 94; peptide 95; peptide 96; peptide 97; peptide 98; peptide 99; peptide 100; peptide 101; peptide 102; peptide 103; peptide 104; and peptide 105; the 10-mers (i.e., peptides having a 10 amino acid sequence): peptide 106; peptide 107; peptide 108; peptide 109; peptide 110; peptide 111; peptide 112; peptide 113; peptide 114; peptide 115; peptide 116; peptide 117; peptide 118; peptide 119; and peptide 120; the 9-mers (i.e., peptides having a 9 amino acid sequence): peptide 121; peptide 122; peptide 123; peptide 124; peptide 125; peptide 126; peptide 127; peptide 128; peptide 129; peptide 130; peptide 131; peptide 132; peptide 133; peptide 134; peptide 135; and peptide 136; the 8-mers (i.e., peptides having a 8 amino acid sequence): peptide 137; peptide 138; peptide 139; peptide 140;

peptide 141; peptide 142; peptide 143; peptide 144; peptide 145; peptide 146; peptide 147; peptide 148; peptide 149; peptide 150; peptide 151; peptide 152; and peptide 153; the 7-mers (i.e., peptides having a 7 amino acid sequence): peptide 154; peptide 155; peptide 156; peptide 157; peptide 158; peptide 159; peptide 160; peptide 161; peptide 162; peptide 163; peptide 164; peptide 165; peptide 166; peptide 167; peptide 168; peptide 169; peptide 170; and peptide 171; the 6-mers (i.e., peptides having a 6 amino acid sequence): peptide 172; peptide 173; peptide 174; peptide 175; peptide 176; peptide 177; peptide 178; peptide 179; peptide 180; peptide 181; peptide 182; peptide 183; peptide 184; peptide 185; peptide 186; peptide 187; peptide 188; peptide 189; and peptide 190; the 5-mers (i.e., peptides having a 5 amino acid sequence): peptide 191; peptide 192; peptide 193; peptide 194; peptide 195; peptide 196; peptide 197; peptide 198; peptide 199; peptide 200; peptide 201; peptide 202; peptide 203; peptide 204; peptide 205; peptide 206; peptide 207; peptide 208; peptide 209; and peptide 210; and the 4-mers (i.e., peptides having a 4 amino acid sequence): peptide 211; peptide 212; peptide 213; peptide 214; peptide 215; peptide 216; peptide 217; peptide 218; peptide 219; peptide 220; peptide 221; peptide 222; peptide 223; peptide 224; peptide 225; peptide 226; peptide 227; peptide 228; peptide 229; peptide 230; and peptide 231.

[0035] Preferred amino acid sequences of isolated peptides and of N-terminal- and/or C-terminal-chemically modified peptides of the current invention are selected from the group consisting of the 23-mens: PEPTIDE 2; and PEPTIDE 3; the 22-mers: PEPTIDE 4; PEPTIDE 5; and PEPTIDE 6; the 21-mers: PEPTIDE 7; PEPTIDE 8; PEPTIDE 9; and PEPTIDE 10; the 20-mers: PEPTIDE 11; PEPTIDE 12; PEPTIDE 13; PEPTIDE 14; and PEPTIDE 15; the 19-mers: PEPTIDE 16; PEPTIDE 17; PEPTIDE 18; PEPTIDE 19; PEPTIDE 20; and PEPTIDE 21; the 18-mers: PEPTIDE 22; PEPTIDE 23; peptide 24; peptide 25; peptide 26; peptide 27; and peptide 28; the 17-mers: peptide 29; peptide 30; peptide 31; peptide 32; peptide 33; peptide 34; peptide 35; and peptide 36; the 16-mers: peptide 37; peptide 38; peptide 39; peptide 40; peptide 41; peptide 42; peptide 43; peptide 44; and peptide 45; the 15-mers: peptide 46; peptide 47; peptide 48; peptide 49; peptide 50; peptide 51; peptide 52; peptide 53; and peptide 54; the 14-mers: peptide 56; peptide 57; peptide 58; peptide 59; peptide 60; peptide 61; peptide 62; peptide 63; and peptide 64; the 13-mers: peptide 67; peptide 68; peptide 69; peptide 70; peptide 71; peptide 72; peptide 73; peptide 74; and peptide 75; the 12-mers: peptide 79; peptide 80; peptide 81; peptide 82; peptide 83; peptide 84; peptide 85; peptide 86; and peptide 87; the 11-mers: peptide 92; peptide 93; peptide 94; peptide 95; peptide 96; peptide 97; peptide 98; peptide 99; and peptide 100; the 10-mers: peptide 106; peptide 107; peptide 108; peptide 109; peptide 110; peptide 111; peptide 112; peptide 113; and peptide 114; the 9-mers: peptide 122; peptide 123; peptide 124; peptide 125; peptide 126; peptide 127; peptide 128; and peptide 129; the 8-mers: peptide 139; peptide 140; peptide 141; peptide 142; peptide 143; peptide 144; and peptide 145; the 7-mers: peptide 157; peptide 158; peptide 159; peptide 160; peptide 161; and peptide 162; the 6-mers: peptide 176; peptide 177; peptide 178; peptide 179; and peptide 180; the 5-mers: peptide 196; peptide 197; peptide 198; and peptide 199; and the 4-mers: peptide 217; and peptide 219.

[0036] More preferred amino acid sequences of isolated peptides and of N-terminal- and/or C-terminal-chemically modified peptides of the current invention are selected from the group consisting of the 23-mers: peptide 2; and peptide 3; the 22-mers: peptide 4; peptide 5; and peptide 6; the 21-mers: peptide 7; peptide 8; peptide 9; and peptide 10; the 20-mers: peptide 11; peptide 12; peptide 13; peptide 14; and peptide 15; the 19-mers: peptide 16; peptide 17; peptide 18; peptide 19; peptide 20; and peptide 21; the 18-mers: peptide 22; peptide 23; peptide 24; peptide 25; peptide 26; peptide 27; and peptide 28; the 17-mers: peptide 29; peptide 30; peptide 31; peptide 32; peptide 33; peptide 34; peptide 35; and peptide 36; the 16-mers: peptide 37; peptide 38; peptide 39; peptide 40; peptide 41; peptide 42; peptide 43; peptide 44; and peptide 45; the 15-mers: peptide 46; peptide 47; peptide 48; peptide 49; peptide 50; peptide 51; peptide 52; peptide 53; and peptide 54; the 14-mers: peptide 56; peptide 57; peptide 58; peptide 59; peptide 60; peptide 61; peptide 62; peptide 63; and peptide 64; the 13-mers: peptide 67; peptide 68; peptide 69; peptide 70; peptide 71; peptide 72;

peptide 73; peptide 74; peptide 80; peptide 81; peptide 82; peptide 83; peptide 84; peptide 85; peptide 86; and peptide 87; the 11-mers: peptide 92; peptide 93; peptide 94; peptide 95; peptide 96; peptide 97; peptide 98; peptide 99; and peptide 100; the 10-mers: peptide 106; peptide 108; peptide 109; peptide 110; peptide 111; peptide 112; peptide 113; and peptide 114; the 9-mers: peptide 124; peptide 125; peptide 126; peptide 127; peptide 128; and peptide 129; the 8-mers: peptide 141; peptide 142; peptide 143; peptide 144; and peptide 145; the 7-mers: peptide 159; peptide 160; peptide 161; and peptide 162; the 6-mers: peptide 178; peptide 179; and peptide 180; the 5-mers: peptide 198; and peptide 199; and the 4-mer: peptide 219.

[0037] In another embodiment, peptide sequences of the current invention have an amino acid sequence selected from the group consisting of (a) an amino acid sequence having from 10 to 23 contiguous amino acids of the reference sequence, peptide 1; (b) a sequence substantially similar to the amino acid sequence defined in (a); and (c) a variant of the amino acid sequence defined in (a), which variant is selected from the group consisting of a substitution variant, a deletion variant, an addition variant, and combinations thereof, wherein the preferred amino acid sequences comprise the 23-mer: peptide 2; the 22-mer: peptide 4; the 21-mer: peptide 7; the 20-mer: peptide 11; the 19-mer: peptide 16; the 18-mer: peptide 22; the 17-mer: peptide 29; the 16-mer: peptide 37; the 15-mer: peptide 46; the 14-mer: peptide 56; the 13-mer: peptide 67; the 12-mer: peptide 79; the 11-mer: peptide 92; and the 10-mer: peptide 106.

[0038] In yet other embodiments, the amino acid sequence of the peptide includes the contiguous residues G, A, Q, F, S, K, T, A, A and K as in peptide 106 of the reference sequence peptide 1. For example, the peptides may have an amino acid sequence selected from the group consisting of (a) an amino acid sequence having from 10 to 23 contiguous amino acids of the reference sequence peptide 1, wherein the amino acid sequence of the peptide includes the contiguous residues G, A, Q, F, S, K, T, A, A and K as in peptide 106 of the reference peptide 1; (b) a sequence with at least about 75%, at least about 80% identity, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, or at least about 95% identity to the amino acid sequence defined in (a); or (c) a variant of the amino acid sequence defined in (a).

[0039] In further embodiments, the amino acid sequence of the peptide begins from the N-terminal amino acid of the reference sequence peptide 1 and includes the contiguous residues G, A, Q, F, S, K, T, A, A and K as in peptide 106 of the reference sequence peptide 1, while in other embodiments the amino acid sequence of the peptide ends at the C-terminal amino acid of the reference sequence peptide 1 and includes the contiguous residues G, A, Q, F, S, K, T, A, A and K as in peptide 106 of the reference sequence peptide 1. In some embodiments, the amino acid sequence of the peptide consists of SEQ ID NO: 106.

[0040] In yet other embodiments, the amino acid sequence of the peptide includes the contiguous residues A, K, G, and E as in peptide 219 of the reference sequence peptide 1. For example, the peptides may have an amino acid sequence selected from the group consisting of (a) an amino acid sequence having from 4 to 23 contiguous amino acids of the reference sequence peptide 1, wherein the amino acid sequence of the peptide includes the contiguous residues A, K, G, and E as in peptide 219 of the reference peptide 1 (e.g., peptide 219, peptide 45, peptide 79, peptide 67, peptide 80, etc.); (b) a sequence with at least about 75%, at least about 80% identity, at least about 85%, at least about 90%, at least about 91%, at least about 92%, at least about 93%, at least about 94%, or at least about 95% identity to the amino acid sequence defined in (a); or (c) a variant of the amino acid sequence defined in (a).

[0041] In further embodiments, the amino acid sequence of the peptide begins from the N-terminal amino acid of the reference sequence peptide 1 and includes the contiguous residues A, K, G, and E as in peptide 219 of the reference sequence peptide 1, while in other embodiments the amino acid sequence of the peptide ends at the C-terminal amino acid of the reference sequence peptide 1 and includes the contiguous residues A, K, G, and E as in peptide 219 of the reference sequence peptide 1. In some embodiments, the amino acid sequence of the peptide consists of SEQ ID NO: 219.

[0042] In exemplary aspects, the peptide is acetylated at the N-terminal amino acid. In exemplary aspects, the peptide comprises or consists of the amino acid sequence of SEQ ID NO: 106 and is acetylated at the N-terminal amino acid. In some aspects, the peptide comprises or consists of the amino acid sequence of SEQ ID NO: 219, and is acetylated at the N-terminal amino acid.
[0043] The peptides may include one or more amino acid deletions, substitutions, and/or additions with respect to the reference amino acid sequence. Preferably, the substitutions may be conservative amino acid substitutions, or the substitutions may be non-conservative amino acid substitutions. In some embodiments, the peptides, including the peptides with amino acid sequences that are substantially identical to or variants of the reference amino acid sequence, will not have deletions or additions as compared to the corresponding contiguous amino acids of the reference amino acid sequence, but may have conservative or non-conservative substitutions. Amino acid substitutions that may be made to the reference amino acid sequence in the peptides of the invention include, but are not limited to, the following: alanine (A) may be substituted with lysine (K), valine (V), leucine (L), or isoleucine (I); glutamic acid (E) may be substituted with aspartic acid (D); glycine (G) may be substituted with proline (P); lysine (K) may be substituted with arginine (R), glutamine (Q), or asparagine (N); phenylalanine (F) may be substituted with leucine (L), valine (V), isoleucine (I), or alanine (A); proline (P) may be substituted with glycine (G); glutamine (Q) may be substituted with glutamic acid (E) or asparagine (N); arginine (R) may be substituted with lysine (K), glutamine (Q), or asparagine (N); serine(S) may be substituted with threonine; threonine (T) may be substituted with serine (S); and valine (V) may be substituted with leucine (L), isoleucine (I), methionine (M), phenylalanine (F), alanine (A), or norleucine (Nle). For example, substitutions that could be made to the reference amino acid sequence in the peptides of the invention include substituting alanine (A) for phenylalanine (F) (e.g., at amino acid position 4 of the reference amino acid sequence), glutamic acid (E) for glutamine (Q) (e.g., at amino acid position 3 of the reference amino acid sequence), lysine (K) for alanine (A) (e.g., at amino acid positions 2 and/or 8 of the reference amino acid sequence), and/or serine(S) for threonine (T) (e.g., at amino acid position 7 of the reference amino acid sequence).
[0044] When substitutions are included in the amino acid sequences of the peptides of the invention (which peptides comprise unmodified as well as peptides which are chemically modified for example by N-terminal and/or C-terminal modification such as by amide formation) with respect to the reference amino acid sequence, there is preferably at least 80% sequence identity between the amino acid sequence of the peptide and the reference amino acid sequence. Peptides having 4 to 23 amino acids and including one amino acid substitution with respect to the reference amino acid sequence will have between about 80% to about 96% (i.e., 95.7%) sequence identity to the reference amino acid sequence. Peptides having 10 to 23 amino acids and including one amino acid substitution with respect to the reference amino acid sequence will have between about 90% to about 96% (i.e., .sup.˜95.7%) sequence identity to the reference amino acid sequence. Peptides having 20 to 23 amino acids and including one amino acid substitution with respect to the reference amino acid sequence will have between about 95% to about 96% (i.e., 95.7%) sequence identity to the reference amino acid sequence. Peptides having 10 to 23 amino acids and including two amino acid substitutions with respect to the reference amino acid sequence will have between about 80% to about 92% (i.e., .sup.˜91.3%) sequence identity to the reference amino acid sequence. Peptides having 16 to 23 amino acids and including two amino acid substitutions with respect to the reference amino acid sequence will have between about 87.5% to about 92% (i.e., ˜91.3%) sequence identity to the reference amino acid sequence. Peptides having 20 to 23 amino acids and including two amino acid substitutions with respect to the reference amino acid sequence will have between about 90% to about 92% (i.e., .sup.˜91.3%) sequence identity to the reference amino acid sequence. Peptides having 15 to 23 amino acids and including three amino acid substitutions with respect to the reference amino acid sequence will have between about 80% to about 87% sequence identity to the reference amino acid sequence. Peptides having 20 to 23 amino acids and including

three amino acid substitutions with respect to the reference amino acid sequence will have between about 85% to about 87% sequence identity to the reference amino acid sequence. Peptides having 20 to 23 amino acids and including four amino acid substitutions with respect to the reference amino acid sequence will have between about 80% to about 83% (i.e., .sup.˜82.6%) sequence identity to the reference amino acid sequence.

[0045] In some embodiments, the present disclosure provides composition comprising the peptides provided herein and salts thereof. For example, in some embodiments, the disclosure encompasses the peptides provided herein and pharmaceutically acceptable salts thereof. Pharmaceutically acceptable salts of the peptides of this disclosure include, for example, peptides modified by making acid or base salts thereof. Examples of acid addition salts include acetate, adipate, alginate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, citrate, camphorate, camphorsulfonate, cyclopentanepropionate, digluconate, dodecylsulfate, ethanesulfonate, fumarate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, lactate, maleate, malonate, methanesulfonate, 2-naphthalenesulfonate, nicotinate, oxalate, palmoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, and undecanoate. Base salts include ammonium salts, alkali metal salts such as sodium and potassium salts, alkaline earth metal salts such as calcium and magnesium salts, salts with organic bases such as dicyclohexylamine salts, N-methyl-D-glutamine, and salts with amino acids such as arginine, lysine, and so forth. Also, the basic nitrogen-containing groups may be quaternized with such agents as lower alkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl; and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides and others.

Pharmaceutical Compositions

[0046] In some aspects, any one of the peptides disclosed herein is contained in a pharmaceutical composition which is useful to prevent, treat, and/or block progression of skin inflammation and/or itch. In some aspects, any one of the peptides disclosed herein is contained in a pharmaceutical composition which is useful to prevent, treat, and/or block progression of a disease or disorder of the skin such as, for example, psoriasis or atopic dermatitis.

[0047] The disclosure also encompasses a composition comprising a peptide as described in the paragraphs above and described herein and an excipient. The disclosure also encompasses a pharmaceutical composition comprising a peptide as described in the paragraphs above and described herein and a pharmaceutically acceptable carrier. The pharmaceutical composition can further preferably be sterile, sterilizable or sterilized. These peptides can be contained in a kit with reagents useful for administration.

[0048] In one aspect, the disclosure relates to a method of administering a pharmaceutical composition. The pharmaceutical composition comprises a therapeutically effective amount of a known compound and a pharmaceutically acceptable carrier. Pharmaceutically acceptable carriers are preferably liquid dosage forms. Liquid preparations may be used and may be prepared in the form of solutions or suspensions, e.g., solutions containing an active ingredient, and a mixture of water, glycerol, and propylene glycol. If desired, such liquid preparations may include one or more of following: thickening agents such as carboxymethylcellulose also may be used as well as other acceptable carriers, the selection of which is known in the art.

[0049] In certain embodiments, the drug product is present in a solid pharmaceutical composition. A solid composition of matter according to the present disclosure may be formed and may be mixed with and/or diluted by an excipient. The solid composition of matter also may be enclosed within a carrier, which may be, for example, in the form of a capsule, sachet, tablet, paper, or other container. When the excipient serves as a diluent, it may be a solid, semi-solid, a gel, or liquid material that acts as a vehicle, carrier, or medium for the composition of matter. For ophthalmic administration, the pharmaceutical formulation with any one of the peptides disclosed herein can be

prepared in the form of an eye drop, eye gel, ointment, ointment, implant, microspheres, or liposomal formulation, or microemulsion.

[0050] Various suitable excipients will be understood by those skilled in the art and may be found in the *National Formulary,* 19:2404-2406 (2000), the disclosure of pages 2404 to 2406 being incorporated herein in their entirety. Examples of suitable excipients include, but are not limited to, starches, gum arabic, calcium silicate, microcrystalline cellulose, methacrylates, shellac, polyvinylpyrrolidone, cellulose, water, and methylcellulose. The drug product formulations additionally can include lubricating agents such as, for example, talc, magnesium stearate and mineral oil; wetting agents; emulsifying and suspending agents; preserving agents such as methyl- and propyl hydroxybenzoates. Polyols, buffers, and inert fillers also may be used. Examples of polyols include, but are not limited to, mannitol, sorbitol, xylitol, sucrose, maltose, glucose, lactose, dextrose, and the like. Suitable buffers include, but are not limited to, phosphate, citrate, tartrate, succinate, and the like. Other inert fillers that may be used include those that are known in the art and are useful in the manufacture of various dosage forms. If desired, the solid formulations may include other components such as bulking agents and/or granulating agents, and the like. The drug products of the disclosure may be formulated so as to provide quick, sustained, or delayed release of the active ingredient after administration to the patient by employing procedures well known in the art.

[0051] In the event that the above pharmaceuticals are to be used for parenteral or intra-peritoneal administration, such a formulation may comprise sterile aqueous injection solutions, non-aqueous injection solutions, or both, comprising the composition of matter of the present disclosure. When aqueous injection solutions are prepared, the composition of matter may be present as a water soluble pharmaceutically acceptable salt. Parenteral or intra-peritoneal preparations may contain anti-oxidants, buffers, bacteriostats, and solutes which render the formulation isotonic with the blood of the intended recipient. Aqueous and non-aqueous sterile suspensions may comprise suspending agents and thickening agents. The formulations may be presented in unit-dose or multi-dose containers, for example sealed ampules and vials. Extemporaneous injection solutions and suspensions may be prepared from sterile powders, granules and tablets of the kind previously described. The parenteral or intra-ocular formulation can also be as liposomal composition.

[0052] The composition of matter also may be formulated such that it may be suitable for topical administration (e.g., ophthalmic drop or gel, or cream). These formulations may contain various excipients known to those skilled in the art. Suitable excipients may include, but are not limited to, cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol, monostearate, methyl stearate, benzyl alcohol, sodium lauryl sulfate, glycerin, mineral oil, water, carbomer, ethyl alcohol, acrylate adhesives, polyisobutylene adhesives, and silicone adhesives.

Methods of Treating Skin Diseases, Disorders or Conditions

[0053] The disclosure provides methods of treating a skin disease, skin disorder or skin condition or one or more symptoms associated with a skin disorder, skin disease or skin condition in a subject by administering to the subject any one of the peptides disclosed herein. In some aspects, the method comprising administering to the subject any one of the peptides listed in Table 1 or Table 1A. In some cases, provided herein are methods for treating, preventing or ameliorating one or more symptoms associated with a skin disease, skin disorder, or skin condition. The one or more symptoms can be selected from the group consisting of skin inflammation, itch or itchiness, scaliness, swelling, rash, thickness, hard patches, dryness, skin flakiness, skin bumps, skin nodules, skin pustules, skin redness, skin ulcers or soars and any combination thereof. The skin disease, skin disorder or skin condition can be selected from the group consisting of acne, alopecia areata, atopic dermatitis (AD, also referred to as eczema), psoriasis, Raynaud's phenomenon, rosacea, vitiligo, actinic prurigo (AP), argyria, chromhidrosis, epidermolysis bullosa, harlequin ichthyosis, lamellar ichthyosis and necrobiosis lipoidica. In some cases, the skin disease, skin disorder or skin condition is an autoinflammatory skin disease such as a neutrophilic dermatoses. Exemplary, but not limiting,

neutrophilic dermatoses that may be treated, prevented or ameliorated via a method provided herein using a peptide provided herein is selected from the group consisting of acute febrile neutrophilic dermatosis (Sweet syndrome), histiocytoid neutrophilic dermatitis, neutrophilic dermatosis of the dorsal hands, pyoderma gangrenosum, neutrophilic eccrine hidradenitis, erythema elevatum diutinum, Behcet disease, bowel bypass syndrome (bowel-associated dermatitis-arthritis syndrome), neutrophilic urticarial dermatosis, palisading neutrophilic granulomatous dermatitis and VEXAS syndrome. In some cases, the neutrophilic dermatoses is pyoderma gangrenosum.

[0054] In some embodiments, the peptide is present in a topical formulation for administration to the surface of the skin. In some embodiments, the peptide is present in a intraperitoneal formulation for administration to the peritoneum of the subject. The disclosure further provides methods of treating a skin disease, skin disorder or skin condition or one or more symptoms associated with a skin disorder, skin disease or skin condition in a subject by administering to the subject a composition comprising any one of the peptides disclosed herein. In embodiments, the peptide comprises or consists of the sequence of SEQ ID NO: 106. In embodiments, the peptide comprises or consists of the sequence of SEQ ID NO: 219.

[0055] In some aspects, the subject is a mammal, such as humans, canines, equines and felines.

[0056] The method of administration of the peptides and compositions disclosed herein may be by topical administration or intraperitoneal (ip) administration or injection. In some embodiments, the method of administration of the peptides and compositions disclosed herein is by a combination of ip injection and topical administration. For example, in some embodiments, the compositions are administered by ip injection followed by topical administration; or by topical administration followed by ip injection. Topical and/or ip administration may be, for example, once daily, twice daily, three times daily, four times daily, or more.

[0057] Additionally, the administration to the subject can further include the administration of a second molecule selected from the group consisting of an antibiotic, an antiviral compound, an antiparasitic compound, an antifungal compound, an antihistamine compound, an anti-inflammatory compound, a corticosteroid, an immunosuppressant, and an immunomodulator. As used herein, an immunomodulator or immunomodulatory compound is an agent that can affect the functioning of the immune system. In some aspects, the immunomodulatory compound helps normalize or regulate the immune system. Non limiting examples of immunomodulators include azathioprine, methotrexate, cyclosporine, tacrolimus, sirolimus, and everolimus.

[0058] In some aspects, the peptide is administered at a concentration from about 1 μM to about 10 mM, such as, for example, about 10 μM, about 20 μM, about 30 μM, about 40 μM, about 50 μM, about 60 μM, about 70 μM, about 80 μM, about 90 μM, about 100 μM, about 150 μM, about 200 μM, about 250 μM, about 300 μM, about 350 μM, about 400 M, about 450 μM, about 500 μM, about 550 μM, about 600 μM, about 650 μM, about 700 μM, about 750 μM, about 800 μM, about 850 μM, about 900 μM, about 950 μM, about 1 mM, about 2 mM, about 3 mM, about 4 mM, about 5 mM, about 6 mM, about 7 mM, about 8 mM, about 9 mM, or about 10 mM, including all subranges and values that lie therebetween.

[0059] In some aspects, the peptide is administered in an amount of about 1 μg to about 5 mg, such as for example, about 10 μg, about 20 μg, about 30 μg, about 40 μg, about 50 μg, about 60 μg, about 70 μg, about 80 μg, about 90 μg, about 100 μg, about 150 μg, about 200 μg, about 250 μg, about 300 μg, about 350 μg, about 400 μg, about 450 μg, about 500 μg, about 550 μg, about 600 μg, about 650 μg, about 700 μg, about 750 μg, about 800 μg, about 850 μg, about 900 μg, about 950 μg, about 1 mg, about 2 mg, about 3 mg, about 4 mg, or about 5 mg, including all subranges and values that lie therebetween.

[0060] In some embodiments, the peptide may be administered in a volume of about 0.01 mL to about 1 mL, such as for example, about 0.01 mL, about 0.05 mL, about 0.1 mL, about 0.5 mL, about 0.75 mL, or about 1 mL, including all subranges and values that lie therebetween.

[0061] The disclosure also provides a composition or formulation for topical or intraperitoneal

administration comprising at least one peptide having an amino acid sequence selected from the group consisting of: (a) an amino acid sequence having from 4 to 24 contiguous amino acids of a reference sequence, GAQFSKTAAKGEAAAERPGEAAVA (SEQ ID NO. 1); (b) an amino acid sequence having the sequence, GAQFSKTAAKGEAAAERPGEAAVA (SEQ ID NO. 1); and (c) an amino acid sequence with at least about 75% identity to the amino acid sequence defined in (a) or (b), for use in a method of treating a skin disease, skin disorder or skin condition or one or more symptoms associated with a skin disorder, skin disease or skin condition in a subject, the method comprising administering the composition to the subject. In embodiments, the peptide has an amino acid sequence according to SEQ ID NO: 106. In embodiments, the peptide is BIO-11006 (Ac-GAQFSKTAAK-OH; SEQ ID NO: 106). In embodiments, the peptide comprises an amino acid sequence of SEQ ID NO: 219. In embodiments, the peptide is BIO-91201 (Ac-AKGE-OH; SEQ ID NO: 219). In embodiments, the peptide is BIO-91202 (Ac-AKGE-NH2; SEQ ID NO: 219). In embodiments, the topical composition or topical formulation is suitable for administration to the skin. In embodiments, the composition or formulation is suitable for administration to the peritoneum.

[0062] Having now described the disclosure, the same will be illustrated with reference to certain examples, which are included herein for illustration purposes only, and which are not intended to be limiting of the disclosure.

EXAMPLES

Example 1. Examination of the Role of MARCKS in Skin Inflammation and Itch in Atopic Dermatitis (AD) and Psoriasis

Objective

[0063] The precise mechanisms of the myristoylated alanine-rich C kinase substrate (MARCKS) protein and its relationship to inflammation and pain/itch remain undefined. Accordingly, an objective of this Example is to determine the role of MARCKS in the regulation and contribution to atopic dermatitis (AD) and psoriasis pathogenesis.

Materials and Methods

[0064] Since skin inflammation and itch are common problems, two different mouse models with inflammation and itch were developed and used for rigorous in vivo testing of the inhibition of skin inflammation and itch in response to administration of the MARCKS inhibitor BIO11006 (Ac-GAQFSKTAAK-OH; SEQ ID NO: 106). The first model is a mouse model of AD induced using MC903. The timeline and drug delivery used for the MC903 induced AD mouse model is shown in FIG. **1**A. The second model is a mouse model of psoriasis induced using imiquimod. Imiquimod-induced disease progression of skin inflammation and itch resemble the MC903 mouse model. As such, the same relative timeline and drug delivery was used for the psoriasis mouse model as described for MC903 mouse model with exception that the terminal day was day 7 (D7 in FIG. **2**A). As outlined in FIGS. **1**A and **2**A, these mouse models were used to conduct a comprehensive examination of how BIO11006 spatially and kinetically changed the skin following the onset of AD-like or psoriasis-like disease symptoms by measuring skin thickness, histological, molecular analysis of inflammatory markers, and itch behavior.

[0065] As shown in FIG. **1**A, in the AD mouse model, a total of four groups of mice (each group consisting of five C57BL/6 mice) were treated with MC903 every day on the dorsal nape of the neck. Given that the significant skin inflammation was expected to start at day 5, BIO11006 (100 μM) was administered by intraperitoneal injection in four (4) different settings as described in FIG. **1**A (i.e., daily single doses from Day 1 through Day 10, Day 4 through Day 10, Days 9 and 10 or just Day 10). The skin thickness was measured at Day 0, 1, 3, 5, 7 and 10. Additionally, the itch behavior was recorded at Day 0 and Day 10.

[0066] As shown in FIG. **2**A, in the psoriasis mouse model, a total of four groups of mice (each group consisting of five C57BL/6 mice) were treated with Imiquimod every day on the dorsal nape of the neck. Given that the significant skin inflammation was expected to start at day 5, BIO11006

(100 μM) was administered by intraperitoneal injection in three (3) different settings as described in FIG. **2**A (i.e., daily single doses from Day 1 through Day 7, Days 6 and 7 or just Day 7). The skin thickness was measured at Day 0, 1, 3, 5, and 7. Additionally, the itch behavior was recorded at Day 0 and Day 7.

Results and Conclusions

[0067] As can be seen in FIG. **2**B, daily administration of BIO 11006 produced a significant decrease in skin thickness at the end of the study in the mouse model of psoriasis. Additionally, the daily administration of BIO 11006 produced visible protection/improvement in the skin on the nape of the neck of the mice in the psoriasis model (see FIG. **3**) as well as significant decreases in skin dryness, flakiness, bumps and redness (see FIG. **4**). Accordingly, MARCKS appears to play a key role in psoriasis and inhibition of MARCKS by administration of peptide inhibitors of MARCKS (e.g., BIO 11006) can ameliorate the skin inflammation and itch associated with psoriasis.

[0068] The results in the mouse model of AD were less conclusive (see FIG. **1**B) and require follow-up.

Example 2. Evaluation of the Expression of MARCKS and Other Cytokines in Mouse Models of AD and Psoriasis

Objective

[0069] Based on a recently published study (Mishra S K et al., Cell Reports, 2020), the autocrine role of TSLP in periostin production in keratinocytes in an AD and allergen mouse model was established. However, the precise role of MARCKS protein in the regulation of pro-inflammatory and inflammatory cytokines in skin keratinocytes in AD and psoriasis remains completely unknown. As such, an objective of this Example is to examine if MARCKS regulates both pro- and inflammatory cytokines and matrix protein, periostin, in AD and psoriasis.

Materials and Methods

[0070] To examine whether expression patterns of MARCKS and other cytokines are altered in skin in normal versus disease models (i.e., AD and psoriasis), immunohistochemical and molecular assays will be combined. More specifically, following the terminal day of the studies on the role of MARCKS in AD and psoriasis using mouse models of said skin diseases in Example 1 (i.e., D7 for psoriasis and D10 for AD as shown in FIGS. **1**A and **2**A), the mice from each group will be euthanized, and will be further subdivided into two groups for histochemical/immunofluorescence and quantification of the genes for MARCKS, a pro-inflammatory protein (i.e., NF-kB), cytokines and extracellular matrix proteins (i.e., IL23, IL17, TSLP, and periostin). To identify the genes that are upregulated in MC903 (AD model) and Imiquimod-induced (Psoriasis model) mice, the treated mice from the respective disease models will be compared with mice with normal skin (without MC903 and Imiquimod application).

Results

[0071] It is expected that there will be an increase in the gene expression of MARCKS, NF-kB, TSLP, periostin, IL23 (for AD), and IL17 (for psoriasis) in the skin of the mouse models for AD and psoriasis compared to normal mice (without MC903 and Imiquimod application).

[0072] The foregoing examples are illustrative of the present disclosure and are not to be construed as limiting thereof. The disclosure is defined by the following claims, with equivalents of the claims to be included therein.

[0073] All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or exemplary language (e.g., “such as”) provided herein, is intended merely to better illuminate the invention and does not pose a limitation on the scope of the invention unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the invention.

[0074] All references, including publications, patent applications, and patents, cited herein are

hereby incorporated by reference to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

Claims

1. A method of treating a skin disease, skin disorder or skin condition or one or more symptoms associated with a skin disorder, skin disease or skin condition in a subject comprising: administering to said subject a therapeutically effective amount of a composition comprising at least one peptide having an amino acid sequence consisting of from 4 to 24 contiguous amino acids of a reference sequence, GAQFSKTAAKGEAAAERPGEAAVA (SEQ ID NO. 1).
2. The method of claim 1, wherein said peptide had an amino acid sequence consisting of ten contiguous amino acid residues of SEQ ID NO: 1.
3. The method of claim 1, wherein said peptide comprises an amino acid sequence of SEQ ID NO: 106 or SEQ ID NO: 219.
4. The method of any one of claims 1-3, wherein said peptide consists of an amino acid sequence of SEQ ID NO: 106.
5. The method of any of claims 1-4, wherein the peptide is myristoylated or acetylated at the N-terminal amino acid.
6. The method of any one of claims 1-5, wherein the peptide is acetylated at the N-terminal amino acid and consists of an amino acid sequence of SEQ ID NO: 106 or SEQ ID NO: 219.
7. The method according to any one of claims 1-6, wherein the composition comprises a pharmaceutically acceptable carrier.
8. The method according to claim 1, wherein said subject is a mammal.
9. The method according to claim 8, wherein said mammal is selected from the group consisting of humans, canines, equines, rodents and felines.
10. The method according to any one of claims 1-9, wherein the composition is administered by topical administration, intravenous injection, intraperitoneal (ip) administration, or any combination thereof.
11. The method according to any one of claims 1-10, wherein the composition is administered intraperitoneally
12. The method of claim 10 or 11, wherein the administration comprises one, two, three, four, five, or six daily.
13. The method according to claim 1, further comprising administration to said subject a second molecule, wherein the second molecule is an antibiotic, an antiviral compound, an antiparasitic compound, an antifungal compound, an antihistamine compound, an anti-inflammatory compound, an immunomodulatory compound, or any combination thereof.
14. The method of any one of claims 1-13, wherein the composition is administered at a concentration from about 1 μM to about 1 mM.
15. The method of any one of claims 1-14, wherein the composition is administered in an amount of about 100 μM.
16. The method of any one of claims 1-15, wherein the composition is administered in a volume of about 0.01 mL to about 1 mL.
17. The method of any one of the above claims, wherein the skin disease, skin disorder or skin condition is psoriasis.
18. The method of any one of the above claims, wherein the one or more symptoms associated with the skin disease, skin disorder or skin condition is selected from the group consisting of skin thickness, skin dryness, skin flakiness, skin bumps, skin nodules, skin pustules, skin ulceration, skin redness and any combination thereof.