

(54)	PEPTIDES AND METHODS OF USE THEREOF IN TREATING SKIN DISEASES		Publication Classification	
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(21)	Appl. No.:	18/859,290	(57)	ABSTRACT
(22)	PCT Filed:	Feb. 24, 2023	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.	
(86)	PCT No.:	PCT/US2023/063271	Specification includes a Sequence Listing.	
	§ 371 (c)(1),			
	(2) Date:	Oct. 23, 2024		
Related U.S. Application Data				
(60)	Provisional application No. 63/334,366, filed on Apr. 25, 2022.			

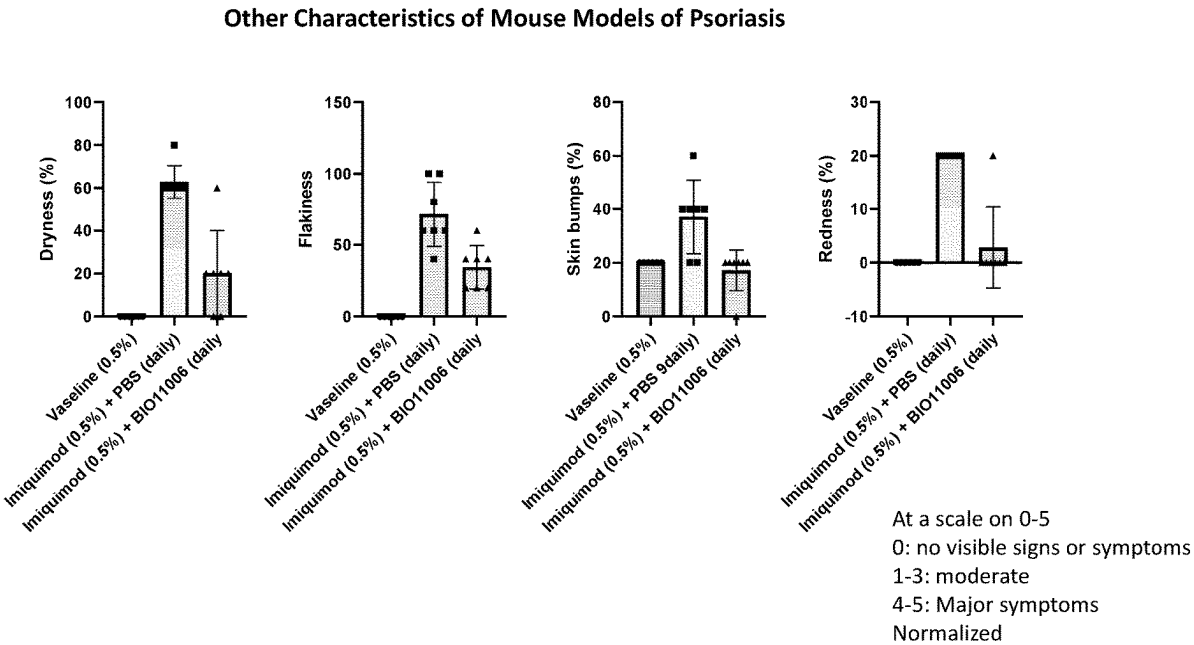
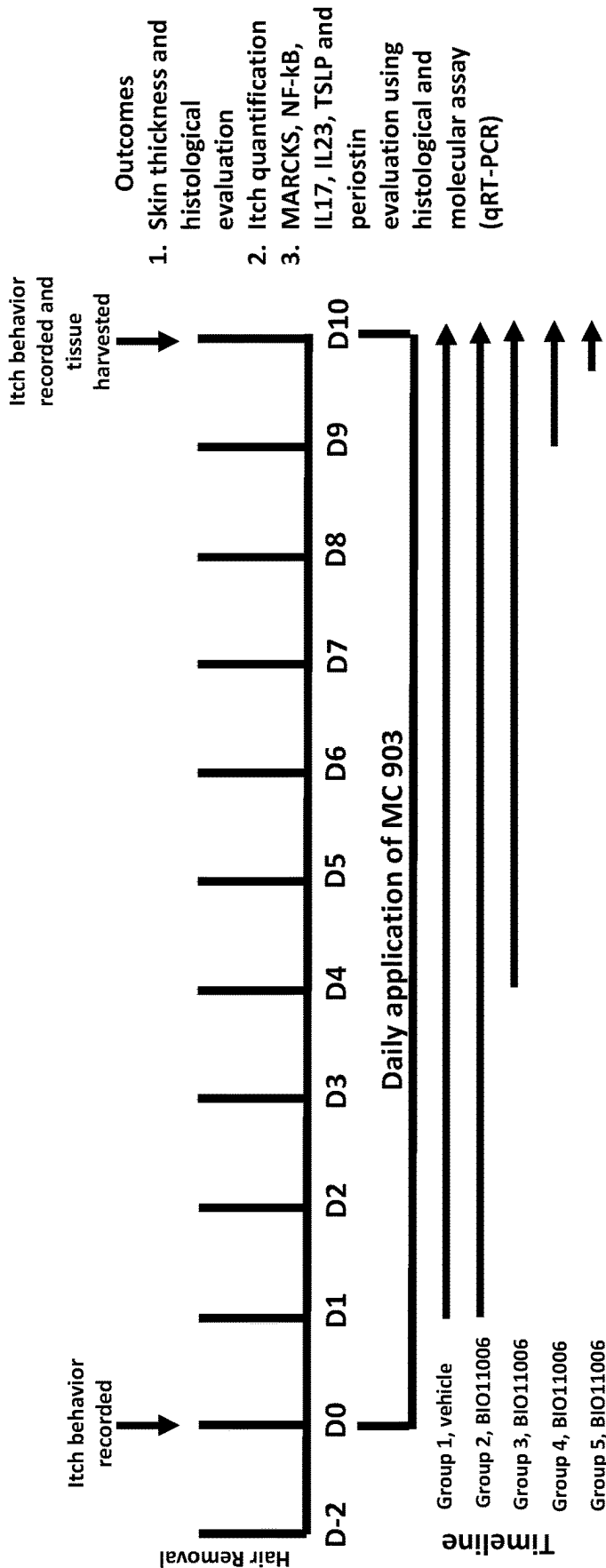


FIG. 1A



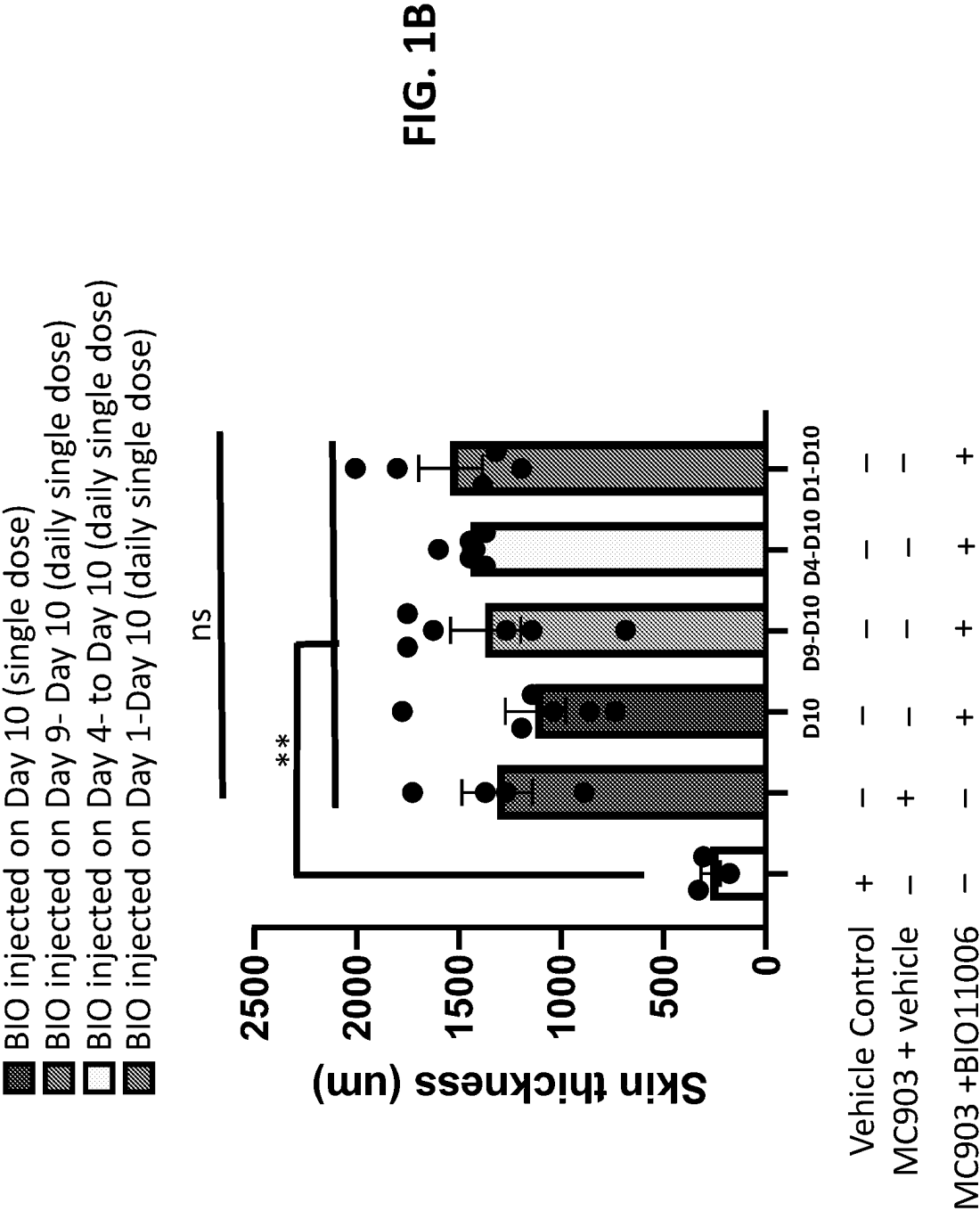
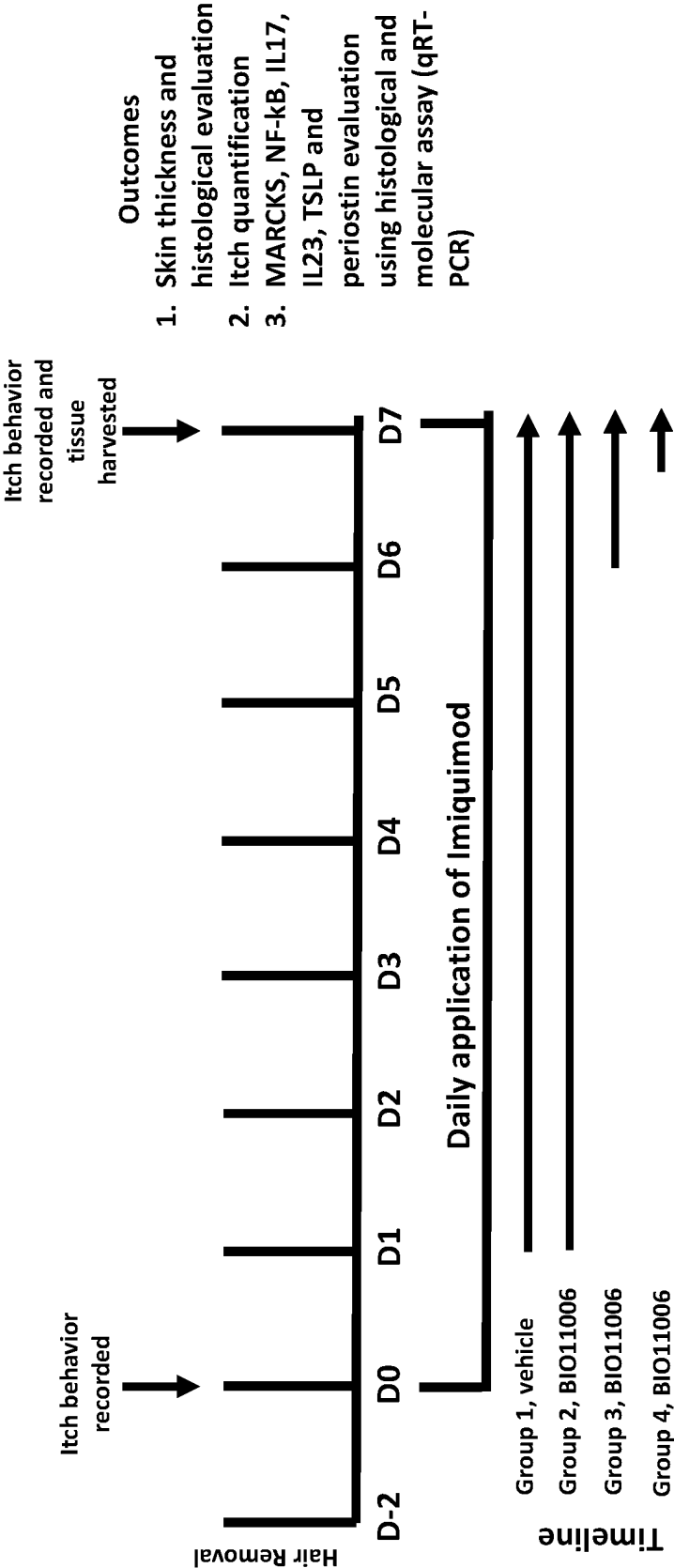


FIG. 2A



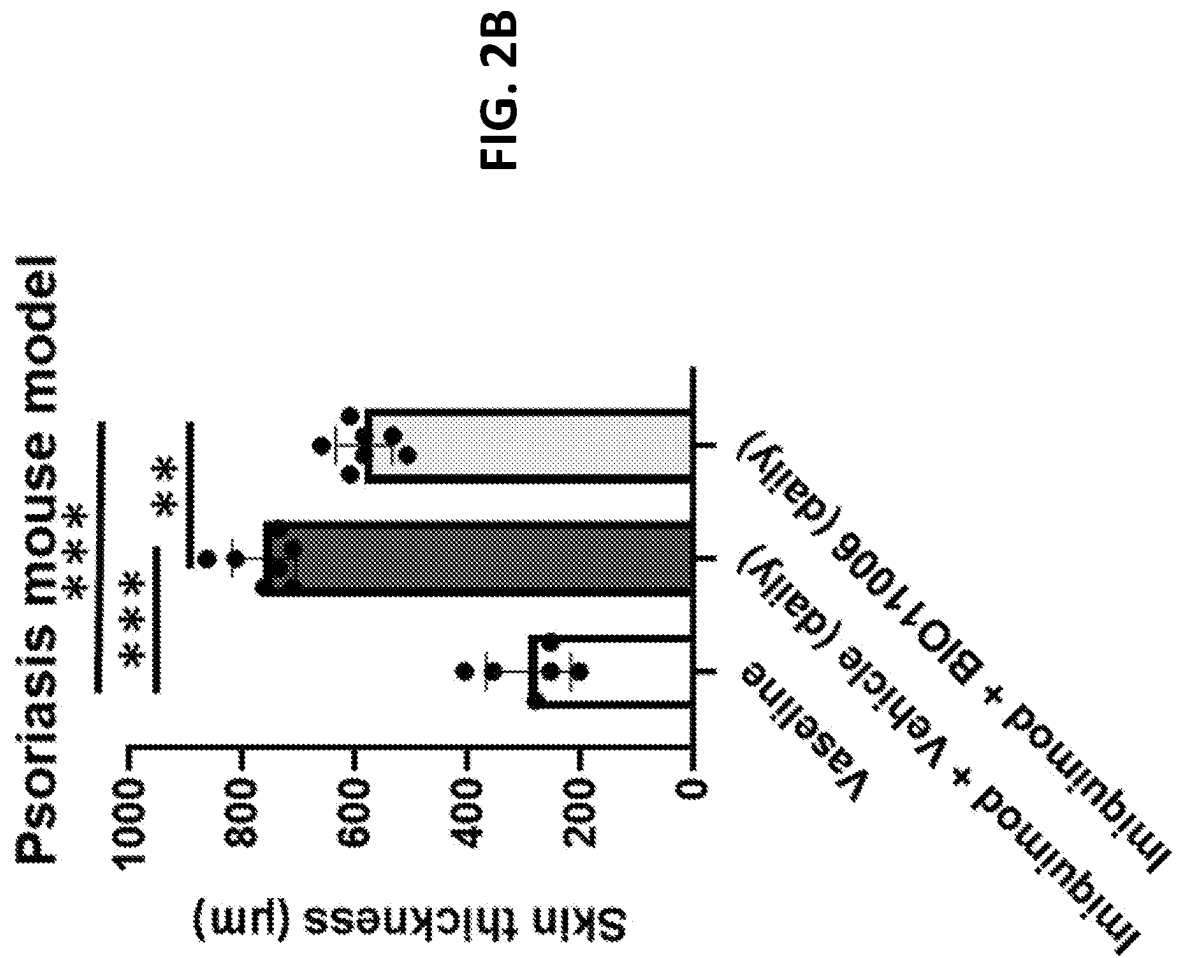
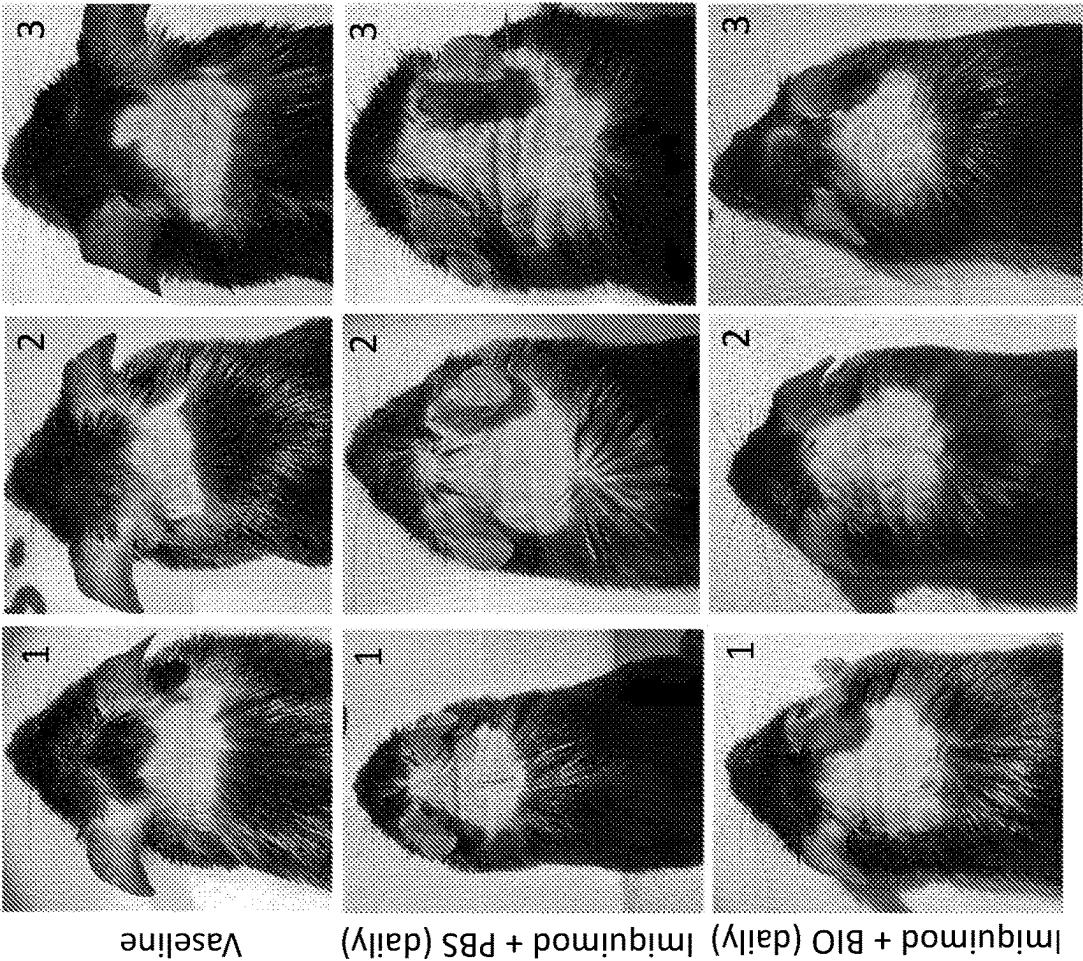


FIG. 2B

N=6-7 mice, mean \pm SD, 1-way ANOVA, Tukey test

Characteristics of Mouse Models of Psoriasis



1, 2 and 3 represent
same treatments

FIG. 3

Other Characteristics of Mouse Models of Psoriasis

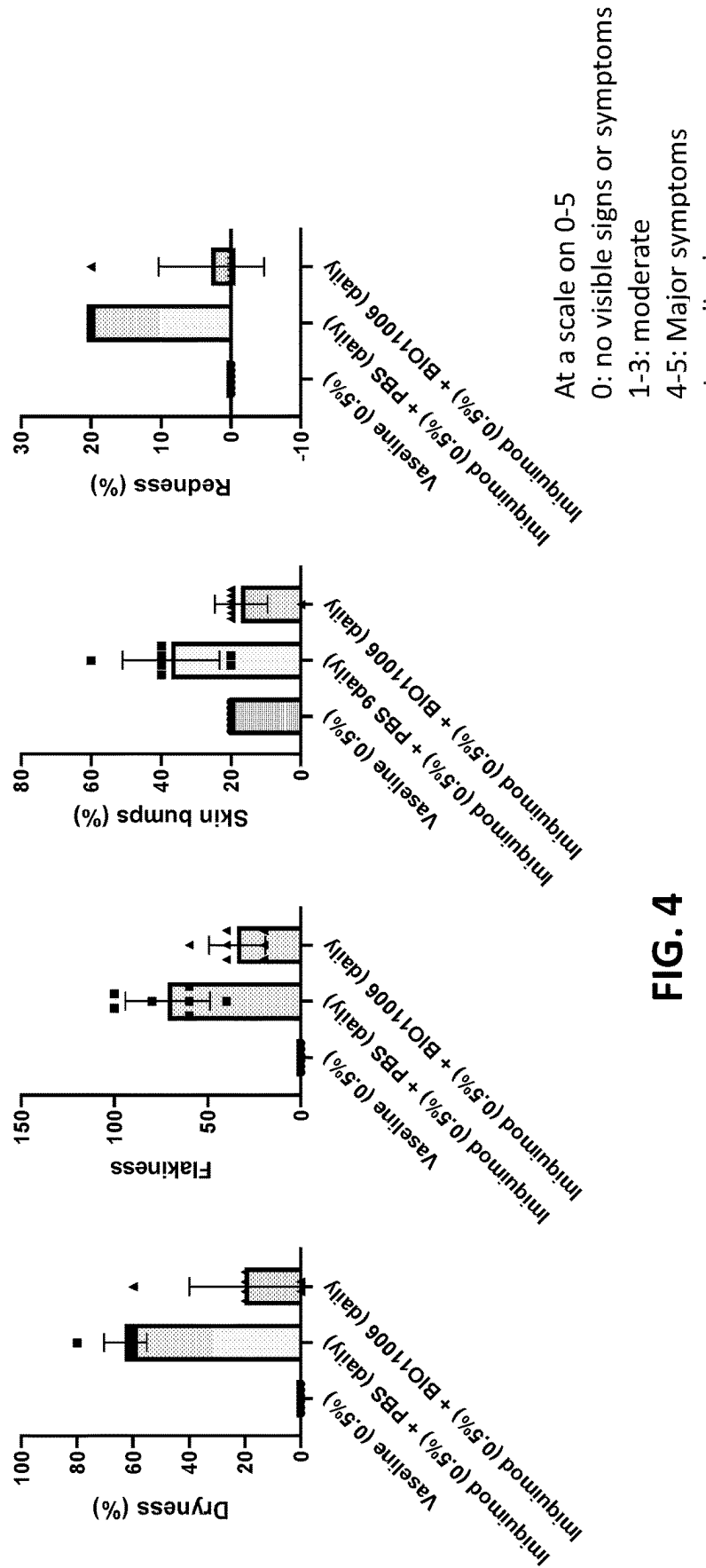


FIG. 4

PEPTIDES AND METHODS OF USE THEREOF IN TREATING SKIN DISEASES

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.

STATEMENT REGARDING FEDERAL FUNDING

[0002] This invention was made with government support under REY030832A awarded by the National Institutes of Health. The government has certain rights in the invention.

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- κ B 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, GAQFSKTAAKGEAAAER-PGEAAVA (SEQ ID NO. 1); (b) an amino acid sequence having the sequence, GAQFSKTAAKGEAAAER-PGEAAVA (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 autoimmune inflammatory skin disease such as a neutrophilic dermatoses. In some cases, the autoimmune inflammatory 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.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIG. 1A 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. 1B 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. 2A 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. 2B 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. 2B 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. 2B 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-GAQFSK-TAAKGEEAAERPGEAAVA (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 1

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
peptide 1	GAQFSKTAAKGEEAAERPGEAAVA	SEQ ID NO. 1
peptide 2	GAQFSKTAAKGEEAAERPGEAAV	SEQ ID NO. 2
peptide 3	AQFSKTAAKGEEAAERPGEAAVA	SEQ ID NO. 3
peptide 4	GAQFSKTAAKGEEAAERPGEAA	SEQ ID NO. 4
peptide 5	AQFSKTAAKGEEAAERPGEAAV	SEQ ID NO. 5
peptide 6	QFSKTAAKGEEAAERPGEAAVA	SEQ ID NO. 6
peptide 7	GAQFSKTAAKGEEAAERPGEA	SEQ ID NO. 7
peptide 8	AQFSKTAAKGEEAAERPGEAA	SEQ ID NO. 8

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
peptide 9	QFSKTAAKGEEAAERPGEAAV	SEQ ID NO. 9
peptide 10	FSKTAAKGEEAAERPGEAAVA	SEQ ID NO. 10
peptide 11	GAQFSKTAAKGEEAAERPGE	SEQ ID NO. 11
peptide 12	AQFSKTAAKGEEAAERPGEA	SEQ ID NO. 12
peptide 13	QFSKTAAKGEEAAERPGEAA	SEQ ID NO. 13
peptide 14	FSKTAAKGEEAAERPGEAAV	SEQ ID NO. 14
peptide 15	SKTAAKGEEAAERPGEAAVA	SEQ ID NO. 15
peptide 16	GAQFSKTAAKGEEAAERPGE	SEQ ID NO. 16
peptide 17	AQFSKTAAKGEEAAERPGE	SEQ ID NO. 17
peptide 18	QFSKTAAKGEEAAERPGEA	SEQ ID NO. 18
peptide 19	FSKTAAKGEEAAERPGEAA	SEQ ID NO. 19
peptide 20	SKTAAKGEEAAERPGEAAV	SEQ ID NO. 20
peptide 21	KTAAKGEEAAERPGEAAVA	SEQ ID NO. 21
peptide 22	GAQFSKTAAKGEEAAERP	SEQ ID NO. 22
peptide 23	AQFSKTAAKGEEAAERPGE	SEQ ID NO. 23
peptide 24	QFSKTAAKGEEAAERPGE	SEQ ID NO. 24
peptide 25	FSKTAAKGEEAAERPGEA	SEQ ID NO. 25
peptide 26	SKTAAKGEEAAERPGEAA	SEQ ID NO. 26
peptide 27	KTAAKGEEAAERPGEAAV	SEQ ID NO. 27
peptide 28	TAAKGEEAAERPGEAAVA	SEQ ID NO. 28
peptide 29	GAQFSKTAAKGEEAAER	SEQ ID NO. 29
peptide 30	AQFSKTAAKGEEAAERP	SEQ ID NO. 30
peptide 31	QFSKTAAKGEEAAERPGE	SEQ ID NO. 31
peptide 32	FSKTAAKGEEAAERPGE	SEQ ID NO. 32
peptide 33	SKTAAKGEEAAERPGEA	SEQ ID NO. 33
peptide 34	KTAAKGEEAAERPGEAA	SEQ ID NO. 34
peptide 35	TAAKGEEAAERPGEAAV	SEQ ID NO. 35
peptide 36	AAKGEEAAERPGEAAVA	SEQ ID NO. 36
peptide 37	GAQFSKTAAKGEEAAE	SEQ ID NO. 37
peptide 38	AQFSKTAAKGEEAAER	SEQ ID NO. 38
peptide 39	QFSKTAAKGEEAAERP	SEQ ID NO. 39
peptide 40	FSKTAAKGEEAAERPGE	SEQ ID NO. 40
peptide 41	SKTAAKGEEAAERPGE	SEQ ID NO. 41
peptide 42	KTAAKGEEAAERPGEA	SEQ ID NO. 42
peptide 43	TAAKGEEAAERPGEAA	SEQ ID NO. 43
peptide 44	AAKGEEAAERPGEAAV	SEQ ID NO. 44

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
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	SKTAAKGEAAAERPGE	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	KTAAKGEAAAERPGE	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	TAAKGEAAAERPGE	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

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
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

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
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

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
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	KGEAAA	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	PGEEAAV	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	GEAAA	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	PGEEAAV	SEQ ID NO. 189
peptide 190	GEAAVA	SEQ ID NO. 190

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
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

TABLE 1-continued

Peptides and Amino Acid Sequences		
Peptide No.	Sequence	Sequence ID No.
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	GTAPAAEGAGA EVKRASAEAKQAF	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	GAEFSTAAKGE	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	GAAPSKTAAK	SEQ ID NO. 243
peptide 244	GAQFAKTAAK	SEQ ID NO. 244
peptide 245	GAQFSATAAK	SEQ ID NO. 245
peptide 246	KAATKSPQAG	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 1A

Peptide Name	Seq ID NO.
MANS	1
Ac-MANS	1
BIO-11211 (Ac—NH ₂)	79
BIO-11000 (Ma—OH)	106
BIO-11002 (Ma—NH ₂)	106
BIO-11005 (H—NH ₂)	106
BIO-11006 (Ac—OH)	106
BIO-11007 (cyclic)	106 cyclic
BIO-11018 (pegylated)	106 pegylated
BIO-11026 (Ac—NH ₂)	106
BIO-10901 (Ac—OH)	121
BIO-10803 (Ac—OH)	137

TABLE 1A-continued

Peptide Name	Seq ID NO.
BIO-91200 (Ma-AKGE-OH)	219
BIO-91201 (Ac-AKGE-OH)	219
BIO-91202 (Ac-AKGE-NH ₂)	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 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). 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-ter-

минаl- 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-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; 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., ~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., ~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., ~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., ~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-naphthalene-sulfonate, 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 the 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 μ M to about 10 mM, such as, for example, about 10 μ M, about 20 μ M, about 30 μ M, about 40 μ M, about 50 μ M, about 60 μ M, about 70 μ M, about 80 μ M, about 90 μ M, about 100 μ M, about 150 μ M, about 200 μ M, about 250 μ M, about 300 μ M, about 350 μ M, about 400 μ M, about 450 μ M, about 500 μ M, about 550 μ M, about 600 μ M, about 650 μ M, about 700 μ M, about 750 μ M, about 800 μ M, about 850 μ M, about 900 μ M, about 950 μ M, 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 μ g to about 5 mg, such as for example, about 10 μ g, about 20 μ g, about 30 μ g, about 40 μ g, about 50 μ g, about 60 μ g, about 70 μ g, about 80 μ g, about 90 μ g, about 100 μ g, about 150 μ g, about 200 μ g, about 250 μ g, about 300 μ g, about 350 μ g, about 400 μ g, about 450 μ g, about 500 μ g, about 550 μ g, about 600 μ g, about 650 μ g, about 700 μ g, about 750 μ g, about 800 μ g, about 850 μ g, about 900 μ g, about 950 μ g, 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, GAQFSKTAAKGEEAAER-PGEAAVA (SEQ ID NO: 1); (b) an amino acid sequence having the sequence, GAQFSKTAAKGEEAAER-PGEAAVA (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. 1A. 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. 2A). As outlined in FIGS. 1A and 2A, 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. 1A, 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 μ M) was administered by intraperitoneal injection in four (4) different settings as described in FIG. 1A (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. 2A, 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 μ M) was administered by intraperitoneal injection in three (3) different settings as described in FIG. 2A (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. 2B, 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. 1B) 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. 1A and 2A), 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.

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SITE	17	
	note = Peptide may or may not be C-term modified	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 33		
SKTAAKGEAA AERPGEA		17
SEQ ID NO: 34	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	17	
	note = Peptide may or may not be C-term modified	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 34		
KTAAKGEAAA ERPGEAA		17
SEQ ID NO: 35	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	17	
	note = Peptide may or may not be C-term modified	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 35		
TAAKGEAAAE RPGEAAV		17
SEQ ID NO: 36	moltype = AA length = 17	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	17	
	note = Peptide may or may not be C-term modified	
source	1..17	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 36		
AAKGEAAAER PGEAAVA		17
SEQ ID NO: 37	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	16	
	note = Peptide may or may not be C-term modified	
source	1..16	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 37		
GAQFSKTAAG EAAAAE		16
SEQ ID NO: 38	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	

-continued

SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 38		
AQFSKTAAGK EAAAER		16
SEQ ID NO: 39	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 39		
QFSKTAAGKE AAAERP		16
SEQ ID NO: 40	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 40		
FSKTAAGKEA AERPGE		16
SEQ ID NO: 41	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 41		
SKTAAGKEAA AERPGE		16
SEQ ID NO: 42	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 42		
KTAAGKEAAA ERPGEA		16
SEQ ID NO: 43	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16 mol_type = protein organism = synthetic construct	
SEQUENCE: 43		
TAAKGEEAAE RPGEAA		16
SEQ ID NO: 44	moltype = AA length = 16	
FEATURE	Location/Qualifiers	
SITE	1	
SITE	note = Peptide may or may not be N-term modified 16	
source	note = Peptide may or may not be C-term modified 1..16	

-continued

SEQUENCE: 44	mol_type = protein
AAKGEEAAER PGAAV	organism = synthetic construct
	16
SEQ ID NO: 45	moltype = AA length = 16
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	16
	note = Peptide may or may not be C-term modified
source	1..16
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 45	
AKGEEAAERP GEEAVA	16
SEQ ID NO: 46	moltype = AA length = 15
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	15
	note = Peptide may or may not be C-term modified
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 46	
GAQFSKTAAG GEEAA	15
SEQ ID NO: 47	moltype = AA length = 15
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	15
	note = Peptide may or may not be C-term modified
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 47	
AQFSKTAAGG EAAAE	15
SEQ ID NO: 48	moltype = AA length = 15
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	15
	note = Peptide may or may not be C-term modified
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 48	
QFSKTAAGGE AAAER	15
SEQ ID NO: 49	moltype = AA length = 15
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	15
	note = Peptide may or may not be C-term modified
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 49	
FSKTAAGGEA AAERP	15
SEQ ID NO: 50	moltype = AA length = 15
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	15
	note = Peptide may or may not be C-term modified
source	1..15
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 50	
SKTAAGGEAA AERPG	15

SEQ ID NO: 51	moltype = AA length = 15	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	15	
	note = Peptide may or may not be C-term modified	
source	1..15	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 51		
KTAAKGEAAA ERPGE		15
SEQ ID NO: 52	moltype = AA length = 15	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	15	
	note = Peptide may or may not be C-term modified	
source	1..15	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 52		
TAAKGEAAAE RPGEA		15
SEQ ID NO: 53	moltype = AA length = 15	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	15	
	note = Peptide may or may not be C-term modified	
source	1..15	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 53		
AAKGEAAAER PGEAA		15
SEQ ID NO: 54	moltype = AA length = 15	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	15	
	note = Peptide may or may not be C-term modified	
source	1..15	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 54		
AKGEAAAERP GEAAV		15
SEQ ID NO: 55	moltype = AA length = 15	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	15	
	note = Peptide may or may not be C-term modified	
source	1..15	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 55		
KGEAAAERPGEA		15
SEQ ID NO: 56	moltype = AA length = 14	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	14	
	note = Peptide may or may not be C-term modified	
source	1..14	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 56		
GAQFSKTAAG		14
SEQ ID NO: 57	moltype = AA length = 14	
FEATURE	Location/Qualifiers	
SITE	1	

-continued

SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14 mol_type = protein organism = synthetic construct	
SEQUENCE: 57 AQFSKTAAKG EAAA		14
SEQ ID NO: 58 FEATURE SITE	moltype = AA length = 14 Location/Qualifiers 1	
SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14 mol_type = protein organism = synthetic construct	
SEQUENCE: 58 QFSKTAAKGE AAAE		14
SEQ ID NO: 59 FEATURE SITE	moltype = AA length = 14 Location/Qualifiers 1	
SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14 mol_type = protein organism = synthetic construct	
SEQUENCE: 59 FSKTAAKGEA AAER		14
SEQ ID NO: 60 FEATURE SITE	moltype = AA length = 14 Location/Qualifiers 1	
SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14 mol_type = protein organism = synthetic construct	
SEQUENCE: 60 SKTAAKGEAA AERP		14
SEQ ID NO: 61 FEATURE SITE	moltype = AA length = 14 Location/Qualifiers 1	
SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14 mol_type = protein organism = synthetic construct	
SEQUENCE: 61 KTAAKGEAAA ERPG		14
SEQ ID NO: 62 FEATURE SITE	moltype = AA length = 14 Location/Qualifiers 1	
SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14 mol_type = protein organism = synthetic construct	
SEQUENCE: 62 TAAKGEAAAE RPGE		14
SEQ ID NO: 63 FEATURE SITE	moltype = AA length = 14 Location/Qualifiers 1	
SITE	note = Peptide may or may not be N-term modified 14	
source	note = Peptide may or may not be C-term modified 1..14	

-continued

SEQUENCE: 63	mol_type = protein	
AAKGEEAAER PGEA	organism = synthetic construct	14
SEQ ID NO: 64	moltype = AA length = 14	
FEATURE	Location/Qualifiers	
REGION	1..14	
	note = Peptide may or may not be C-term and/or N-term modified	
source	1..14	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 64		
AKGEEAAERP GEAA		14
SEQ ID NO: 65	moltype = AA length = 14	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	14	
	note = Peptide may or may not be C-term modified	
source	1..14	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 65		
KGEEAAERPG EAAV		14
SEQ ID NO: 66	moltype = AA length = 14	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	14	
	note = Peptide may or may not be C-term modified	
source	1..14	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 66		
GEAAERPG EAVA		14
SEQ ID NO: 67	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 67		
GAQFSKTAAK GEA		13
SEQ ID NO: 68	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 68		
AQFSKTAAKG EAA		13
SEQ ID NO: 69	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 69		
QFSKTAAKGE AAA		13

-continued

SEQ ID NO: 70	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 70		
FSKTAAKGEA AAE		13
SEQ ID NO: 71	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 71		
SKTAAKGEAA AER		13
SEQ ID NO: 72	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 72		
KTAAKGEAAA ERP		13
SEQ ID NO: 73	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 73		
TAAKGEEAAE RPG		13
SEQ ID NO: 74	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 74		
AAKGEEAAER PGE		13
SEQ ID NO: 75	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 75		
AKGEEAAERP GEA		13
SEQ ID NO: 76	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	

-continued

SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 76		
KGEAAAERPGE EAA		13
SEQ ID NO: 77	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 77		
GEAAAERPGE AAV		13
SEQ ID NO: 78	moltype = AA length = 13	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	13	
	note = Peptide may or may not be C-term modified	
source	1..13	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 78		
EAAAERPGEA AVA		13
SEQ ID NO: 79	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 79		
GAQFSKTAAG GE		12
SEQ ID NO: 80	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 80		
AQFSKTAAGK EA		12
SEQ ID NO: 81	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 81		
QFSKTAAGKGE AA		12
SEQ ID NO: 82	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	

-continued

SEQUENCE: 82	organism = synthetic construct	
FSKTAAKGEA AA		12
SEQ ID NO: 83	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 83		
SKTAAKGEAA AE		12
SEQ ID NO: 84	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 84		
KTAAKGEAAA ER		12
SEQ ID NO: 85	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 85		
TAAKGEAAAE RP		12
SEQ ID NO: 86	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 86		
AAKGEAAAER PG		12
SEQ ID NO: 87	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 87		
AKGEAAAERP GE		12
SEQ ID NO: 88	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 88		
KGEAAAERPG EA		12

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SEQ ID NO: 89	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 89		
GEAAAERPGE AA		12
SEQ ID NO: 90	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 90		
EAAAERPGEA AV		12
SEQ ID NO: 91	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 91		
AAAERPGEAA VA		12
SEQ ID NO: 92	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 92		
GAQFSKTAAG G		11
SEQ ID NO: 93	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 93		
AQFSKTAAG E		11
SEQ ID NO: 94	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 94		
QFSKTAAG E A		11
SEQ ID NO: 95	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	

-continued

SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 95		
FSKTAAKGEEA A		11
SEQ ID NO: 96	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 96		
SKTAAKGEEA A		11
SEQ ID NO: 97	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 97		
KTAAKGEEAA E		11
SEQ ID NO: 98	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 98		
TAAKGEEAAE R		11
SEQ ID NO: 99	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 99		
AAKGEEAAER P		11
SEQ ID NO: 100	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 100		
AKGEEAAERP G		11
SEQ ID NO: 101	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	

-continued

SEQUENCE: 101	organism = synthetic construct	
KGAAAERPG E		11
SEQ ID NO: 102	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 102		
GEAAAERPGE A		11
SEQ ID NO: 103	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 103		
EAAAERPGEA A		11
SEQ ID NO: 104	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 104		
AAAERPGEAA V		11
SEQ ID NO: 105	moltype = AA length = 11	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	11	
	note = Peptide may or may not be C-term modified	
source	1..11	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 105		
AAERPGEAAV A		11
SEQ ID NO: 106	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 106		
GAQFSKTAAK		10
SEQ ID NO: 107	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 107		
AQFSKTAAKG		10

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SEQ ID NO: 108	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 108		
QFSKTAAKGE		10
SEQ ID NO: 109	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 109		
FSKTAAKGEA		10
SEQ ID NO: 110	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 110		
SKTAAKGEAA		10
SEQ ID NO: 111	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 111		
KTAAKGEAAA		10
SEQ ID NO: 112	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 112		
TAAKGEAAAE		10
SEQ ID NO: 113	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 113		
AAKGEAAAER		10
SEQ ID NO: 114	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	

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SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 114 AKGEAAAERP	10
SEQ ID NO: 115 FEATURE SITE	moltype = AA length = 10 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 115 KGEAAAERP	10
SEQ ID NO: 116 FEATURE SITE	moltype = AA length = 10 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 116 GEAAAERPGE	10
SEQ ID NO: 117 FEATURE SITE	moltype = AA length = 10 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 117 EAAAERPGEA	10
SEQ ID NO: 118 FEATURE SITE	moltype = AA length = 10 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 118 AAAERPGEAA	10
SEQ ID NO: 119 FEATURE SITE	moltype = AA length = 10 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein organism = synthetic construct
SEQUENCE: 119 AAERPGEAAV	10
SEQ ID NO: 120 FEATURE SITE	moltype = AA length = 10 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	10
source	note = Peptide may or may not be C-term modified 1..10 mol_type = protein

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SEQUENCE: 120	organism = synthetic construct	
AERPGEAAVA		10
SEQ ID NO: 121	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	9	
	note = Peptide may or may not be C-term modified	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 121		
GAQFSKTAA		9
SEQ ID NO: 122	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	9	
	note = Peptide may or may not be C-term modified	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 122		
AQFSKTAAK		9
SEQ ID NO: 123	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	9	
	note = Peptide may or may not be C-term modified	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 123		
QFSKTAAGK		9
SEQ ID NO: 124	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	9	
	note = Peptide may or may not be C-term modified	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 124		
FSKTAAGKE		9
SEQ ID NO: 125	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	9	
	note = Peptide may or may not be C-term modified	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 125		
SKTAAGGEA		9
SEQ ID NO: 126	moltype = AA length = 9	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	9	
	note = Peptide may or may not be C-term modified	
source	1..9	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 126		
KTAAGGEAA		9

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SEQ ID NO: 127	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	9
	note = Peptide may or may not be C-term modified
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 127	
TAAKGEEAAA	9
SEQ ID NO: 128	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	9
	note = Peptide may or may not be C-term modified
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 128	
AAKGEEAAAE	9
SEQ ID NO: 129	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	9
	note = Peptide may or may not be C-term modified
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 129	
AKGEEAAER	9
SEQ ID NO: 130	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	9
	note = Peptide may or may not be C-term modified
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 130	
KGEEAAERP	9
SEQ ID NO: 131	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	9
	note = Peptide may or may not be C-term modified
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 131	
GEAAERPGE	9
SEQ ID NO: 132	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	9
	note = Peptide may or may not be C-term modified
source	1..9
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 132	
EAAERPGE	9
SEQ ID NO: 133	moltype = AA length = 9
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified

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SITE	9
source	note = Peptide may or may not be C-term modified 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 133 AAAERPGEA	9
SEQ ID NO: 134 FEATURE SITE	moltype = AA length = 9 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	9
source	note = Peptide may or may not be C-term modified 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 134 AAERPGEAA	9
SEQ ID NO: 135 FEATURE SITE	moltype = AA length = 9 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	9
source	note = Peptide may or may not be C-term modified 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 135 AERPGEAAV	9
SEQ ID NO: 136 FEATURE SITE	moltype = AA length = 9 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	9
source	note = Peptide may or may not be C-term modified 1..9 mol_type = protein organism = synthetic construct
SEQUENCE: 136 ERPGEAAVA	9
SEQ ID NO: 137 FEATURE SITE	moltype = AA length = 8 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	8
source	note = Peptide may or may not be C-term modified 1..8 mol_type = protein organism = synthetic construct
SEQUENCE: 137 GAQFSKTA	8
SEQ ID NO: 138 FEATURE SITE	moltype = AA length = 8 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	8
source	note = Peptide may or may not be C-term modified 1..8 mol_type = protein organism = synthetic construct
SEQUENCE: 138 AQFSKTAA	8
SEQ ID NO: 139 FEATURE SITE	moltype = AA length = 8 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	8
source	note = Peptide may or may not be C-term modified 1..8 mol_type = protein

-continued

SEQUENCE: 139	organism = synthetic construct	
QFSKTAAK		8
SEQ ID NO: 140	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 140		
FSKTAAKG		8
SEQ ID NO: 141	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 141		
SKTAAKGE		8
SEQ ID NO: 142	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 142		
KTAAKGEA		8
SEQ ID NO: 143	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 143		
TAAKGEAA		8
SEQ ID NO: 144	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 144		
AAKGEAAA		8
SEQ ID NO: 145	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 145		
AKGEAAAE		8

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SEQ ID NO: 146	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	8
	note = Peptide may or may not be C-term modified
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 146	
KGEAAAER	8
SEQ ID NO: 147	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	8
	note = Peptide may or may not be C-term modified
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 147	
GEAAAERP	8
SEQ ID NO: 148	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	8
	note = Peptide may or may not be C-term modified
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 148	
EAAAERPG	8
SEQ ID NO: 149	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	8
	note = Peptide may or may not be C-term modified
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 149	
AAAERPGE	8
SEQ ID NO: 150	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	8
	note = Peptide may or may not be C-term modified
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 150	
AAERPGEA	8
SEQ ID NO: 151	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	8
	note = Peptide may or may not be C-term modified
source	1..8
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 151	
AERPGEAA	8
SEQ ID NO: 152	moltype = AA length = 8
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified

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SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 152		
ERPGEAAV		8
SEQ ID NO: 153	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 153		
RPGEAAVA		8
SEQ ID NO: 154	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 154		
GAQFSKT		7
SEQ ID NO: 155	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 155		
AQFSKTA		7
SEQ ID NO: 156	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 156		
QFSKTAA		7
SEQ ID NO: 157	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 157		
FSKTAAK		7
SEQ ID NO: 158	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	

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SEQUENCE: 158	organism = synthetic construct	
SKTAAKG		7
SEQ ID NO: 159	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 159		
KTAAKGE		7
SEQ ID NO: 160	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 160		
TAAKGEEA		7
SEQ ID NO: 161	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 161		
AAKGEEAA		7
SEQ ID NO: 162	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 162		
AKGEEAAA		7
SEQ ID NO: 163	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 163		
KGEAAAAE		7
SEQ ID NO: 164	moltype = AA length = 7	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	7	
	note = Peptide may or may not be C-term modified	
source	1..7	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 164		
GEAAAAER		7

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SEQ ID NO: 165	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	7
	note = Peptide may or may not be C-term modified
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 165	
EAAAERP	7
SEQ ID NO: 166	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	7
	note = Peptide may or may not be C-term modified
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 166	
AAAERPG	7
SEQ ID NO: 167	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	7
	note = Peptide may or may not be C-term modified
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 167	
AAERPGE	7
SEQ ID NO: 168	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	7
	note = Peptide may or may not be C-term modified
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 168	
AERPGEA	7
SEQ ID NO: 169	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	7
	note = Peptide may or may not be C-term modified
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 169	
ERPGEAA	7
SEQ ID NO: 170	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	7
	note = Peptide may or may not be C-term modified
source	1..7
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 170	
RPGEAAV	7
SEQ ID NO: 171	moltype = AA length = 7
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified

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SITE	7
source	note = Peptide may or may not be C-term modified 1..7 mol_type = protein organism = synthetic construct
SEQUENCE: 171	
PGEAAVA	7
SEQ ID NO: 172	moltype = AA length = 6
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	6
	note = Peptide may or may not be C-term modified
source	1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 172	
GAQFSK	6
SEQ ID NO: 173	moltype = AA length = 6
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	6
	note = Peptide may or may not be C-term modified
source	1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 173	
AQFSKT	6
SEQ ID NO: 174	moltype = AA length = 6
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	6
	note = Peptide may or may not be C-term modified
source	1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 174	
QFSKTA	6
SEQ ID NO: 175	moltype = AA length = 6
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	6
	note = Peptide may or may not be C-term modified
source	1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 175	
FSKTAA	6
SEQ ID NO: 176	moltype = AA length = 6
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	6
	note = Peptide may or may not be C-term modified
source	1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 176	
SKTAAK	6
SEQ ID NO: 177	moltype = AA length = 6
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	6
	note = Peptide may or may not be C-term modified
source	1..6 mol_type = protein

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SEQUENCE: 177	organism = synthetic construct	
KTAAKG		6
SEQ ID NO: 178	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 178		
TAAKGE		6
SEQ ID NO: 179	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 179		
AAKGEA		6
SEQ ID NO: 180	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 180		
AKGEAA		6
SEQ ID NO: 181	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 181		
KGEAAA		6
SEQ ID NO: 182	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 182		
GEAAAE		6
SEQ ID NO: 183	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 183		
EAAAER		6

-continued

SEQ ID NO: 184	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 184		
AAAERP		6
SEQ ID NO: 185	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 185		
AAERPG		6
SEQ ID NO: 186	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 186		
AERPGE		6
SEQ ID NO: 187	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 187		
ERPGEA		6
SEQ ID NO: 188	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 188		
RPGEAA		6
SEQ ID NO: 189	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	6	
	note = Peptide may or may not be C-term modified	
source	1..6	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 189		
PGEAAV		6
SEQ ID NO: 190	moltype = AA length = 6	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	

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SITE	6
source	note = Peptide may or may not be C-term modified 1..6 mol_type = protein organism = synthetic construct
SEQUENCE: 190 GEAAVA	6
SEQ ID NO: 191 FEATURE SITE	moltype = AA length = 5 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	5 note = Peptide may or may not be C-term modified
source	1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 191 GAQFS	5
SEQ ID NO: 192 FEATURE SITE	moltype = AA length = 5 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	5 note = Peptide may or may not be C-term modified
source	1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 192 AQFSK	5
SEQ ID NO: 193 FEATURE SITE	moltype = AA length = 5 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	5 note = Peptide may or may not be C-term modified
source	1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 193 QFSKT	5
SEQ ID NO: 194 FEATURE SITE	moltype = AA length = 5 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	5 note = Peptide may or may not be C-term modified
source	1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 194 FSKTA	5
SEQ ID NO: 195 FEATURE SITE	moltype = AA length = 5 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	5 note = Peptide may or may not be C-term modified
source	1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 195 SKTAA	5
SEQ ID NO: 196 FEATURE SITE	moltype = AA length = 5 Location/Qualifiers 1 note = Peptide may or may not be N-term modified
SITE	5 note = Peptide may or may not be C-term modified
source	1..5 mol_type = protein

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SEQUENCE: 196	organism = synthetic construct	
KTAAK		5
SEQ ID NO: 197	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	5	
	note = Peptide may or may not be C-term modified	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 197		
TAAKG		5
SEQ ID NO: 198	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	5	
	note = Peptide may or may not be C-term modified	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 198		
AAKGE		5
SEQ ID NO: 199	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	5	
	note = Peptide may or may not be C-term modified	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 199		
AKGEA		5
SEQ ID NO: 200	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	5	
	note = Peptide may or may not be C-term modified	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 200		
KGEAA		5
SEQ ID NO: 201	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	5	
	note = Peptide may or may not be C-term modified	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 201		
GEAAA		5
SEQ ID NO: 202	moltype = AA length = 5	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	5	
	note = Peptide may or may not be C-term modified	
source	1..5	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 202		
EAAAE		5

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SEQ ID NO: 203	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	5
	note = Peptide may or may not be C-term modified
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 203	
AAAER	5
SEQ ID NO: 204	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	5
	note = Peptide may or may not be C-term modified
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 204	
AAERP	5
SEQ ID NO: 205	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	5
	note = Peptide may or may not be C-term modified
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 205	
AERPG	5
SEQ ID NO: 206	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	5
	note = Peptide may or may not be C-term modified
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 206	
ERPGE	5
SEQ ID NO: 207	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	5
	note = Peptide may or may not be C-term modified
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 207	
RPGEA	5
SEQ ID NO: 208	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	5
	note = Peptide may or may not be C-term modified
source	1..5
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 208	
PGEAA	5
SEQ ID NO: 209	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified

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SITE	5
source	note = Peptide may or may not be C-term modified 1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 209	
GAAAV	5
SEQ ID NO: 210	moltype = AA length = 5
FEATURE	Location/Qualifiers
SITE	1
SITE	note = Peptide may or may not be N-term modified 5
source	note = Peptide may or may not be C-term modified 1..5 mol_type = protein organism = synthetic construct
SEQUENCE: 210	
EAAVA	5
SEQ ID NO: 211	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
SITE	note = Peptide may or may not be N-term modified 4
source	note = Peptide may or may not be C-term modified 1..4 mol_type = protein organism = synthetic construct
SEQUENCE: 211	
GAQF	4
SEQ ID NO: 212	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
SITE	note = Peptide may or may not be N-term modified 4
source	note = Peptide may or may not be C-term modified 1..4 mol_type = protein organism = synthetic construct
SEQUENCE: 212	
AQFS	4
SEQ ID NO: 213	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
SITE	note = Peptide may or may not be N-term modified 4
source	note = Peptide may or may not be C-term modified 1..4 mol_type = protein organism = synthetic construct
SEQUENCE: 213	
QFSK	4
SEQ ID NO: 214	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
SITE	note = Peptide may or may not be N-term modified 4
source	note = Peptide may or may not be C-term modified 1..4 mol_type = protein organism = synthetic construct
SEQUENCE: 214	
FSKT	4
SEQ ID NO: 215	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
SITE	note = Peptide may or may not be N-term modified 4
source	note = Peptide may or may not be C-term modified 1..4 mol_type = protein

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SEQUENCE: 215	organism = synthetic construct	
SKTA		4
SEQ ID NO: 216	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 216		
KTAA		4
SEQ ID NO: 217	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 217		
TAAK		4
SEQ ID NO: 218	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 218		
AAKG		4
SEQ ID NO: 219	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 219		
AKGE		4
SEQ ID NO: 220	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 220		
KGEA		4
SEQ ID NO: 221	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 221		
GEAA		4

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SEQ ID NO: 222	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	4
	note = Peptide may or may not be C-term modified
source	1..4
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 222	
EAAA	4
SEQ ID NO: 223	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	4
	note = Peptide may or may not be C-term modified
source	1..4
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 223	
AAAE	4
SEQ ID NO: 224	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	4
	note = Peptide may or may not be C-term modified
source	1..4
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 224	
AAER	4
SEQ ID NO: 225	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	4
	note = Peptide may or may not be C-term modified
source	1..4
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 225	
AERP	4
SEQ ID NO: 226	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	4
	note = Peptide may or may not be C-term modified
source	1..4
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 226	
ERPG	4
SEQ ID NO: 227	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified
SITE	4
	note = Peptide may or may not be C-term modified
source	1..4
	mol_type = protein
	organism = synthetic construct
SEQUENCE: 227	
RPGE	4
SEQ ID NO: 228	moltype = AA length = 4
FEATURE	Location/Qualifiers
SITE	1
	note = Peptide may or may not be N-term modified

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SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 228		
PGEA		4
SEQ ID NO: 229	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 229		
GEAA		4
SEQ ID NO: 230	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 230		
EAAV		4
SEQ ID NO: 231	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 231		
AAVA		4
SEQ ID NO: 232	moltype = AA length = 24	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	24	
	note = Peptide may or may not be C-term modified	
source	1..24	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 232		
GTAPAAEGAG AEVKRASAEA KQAF		24
SEQ ID NO: 233	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 233		
GKQFSKTAAG GE		12
SEQ ID NO: 234	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	

-continued

SEQUENCE: 234	organism = synthetic construct	
GAQFSKTKAK GE		12
SEQ ID NO: 235	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 235		
GKQFSKTKAK GE		12
SEQ ID NO: 236	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 236		
GAQASKTAAK		10
SEQ ID NO: 237	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 237		
GAQASKTAAK GE		12
SEQ ID NO: 238	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 238		
GAEFSKTAAG GE		12
SEQ ID NO: 239	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 239		
GAQFSKTAAA GE		12
SEQ ID NO: 240	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 240		
GAQFSKTAAG AE		12

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SEQ ID NO: 241	moltype = AA length = 12	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	12	
	note = Peptide may or may not be C-term modified	
source	1..12	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 241		
GAQFSKTAAK	GA	12
SEQ ID NO: 242	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 242		
AAQFSKTAAK		10
SEQ ID NO: 243	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 243		
GAAFSKTAAK		10
SEQ ID NO: 244	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 244		
GAQFAKTAAK		10
SEQ ID NO: 245	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 245		
GAQFSATAAK		10
SEQ ID NO: 246	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 246		
KAATKSFQAG		10
SEQ ID NO: 247	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	

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SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 247		
GAQFSKAAAK		10
SEQ ID NO: 248	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 248		
GAQFSKTAAA		10
SEQ ID NO: 249	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 249		
GAQFSATAAA		10
SEQ ID NO: 250	moltype = AA length = 8	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	8	
	note = Peptide may or may not be C-term modified	
source	1..8	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 250		
GAQASKTA		8
SEQ ID NO: 251	moltype = AA length = 4	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	4	
	note = Peptide may or may not be C-term modified	
source	1..4	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 251		
AAGE		4
SEQ ID NO: 252	moltype = AA length = 10	
FEATURE	Location/Qualifiers	
SITE	1	
	note = Peptide may or may not be N-term modified	
SITE	10	
	note = Peptide may or may not be C-term modified	
source	1..10	
	mol_type = protein	
	organism = synthetic construct	
SEQUENCE: 252		
GKASQFAKTA		10

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, GAQFSKTAAKGEEAAERPGEAAVA (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 μ M 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 μ M.

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.

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