

Innate immune defense system of the skin

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Background – Antimicrobial peptides (AMPs) have a pivotal role in cutaneous innate immunity. They are present in the skin of many animals, including mammals, and are both constitutively present and inducible by infection and injury.

Functions – Antimicrobial peptides exhibit antimicrobial activity against bacteria, viruses, fungi and parasites, with different potencies depending on their peptide structure. They also act as multifunctional effector molecules that influence diverse cellular processes, including cell migration, proliferation and differentiation, cytokine production, angiogenesis and wound healing. Suppressed AMP production has been associated with increased susceptibility to microbial insults and the pathogenesis of atopic dermatitis.

This review highlights recent observations on the expression and role of AMPs, particularly the AMPs cathelicidin and β -defensin, in healthy and diseased skin.

Introduction

Skin is the largest organ of the body and provides an effective immune barrier between the internal and external environment. The cutaneous immune system can be arbitrarily divided into innate and adaptive components.¹ The innate immune system of the skin is the first-line, fast, nonspecific and active mechanism against environmental toxins and invading microbes. The innate immune response is followed by acquired immune responses, particularly T- and B-cell activation and proliferation against specific antigens.^{1–3}

The innate immune system of the skin is comprised of both a physical and a chemical shield. The uppermost layer of the epidermis, the stratum corneum, consists of keratinocytes tightly linked by desmosomes in a hydrophobic cellular matrix, thereby creating an anatomical barrier against irritants, allergens and shear force.^{4–6} In addition to an immediate physical barrier, this intrinsic resistance system functions through chemical mediators (cytokines), specialized signalling pathways, the complement cascade, leukocytes and host defense peptides [antimicrobial peptides (AMPs)]. In particular, AMP production is a critical mechanism for immune response of the skin to cutaneous infection and injury. This review discusses the seminal role of AMPs in skin innate immunity.

Antimicrobial peptides

Antimicrobial peptides are evolutionarily conserved major contributors to host innate immune defense against bacteria, viruses, fungi, parasites and tumour cells.^{3,7,8} Over 1700 AMPs are currently known.⁹ They have been described in plants, insects, invertebrates and vertebrates;¹⁰ however, great variability among species exists in AMP tissue distribution, genetic make-up and regulation of expression.¹¹ These differences suggest that AMPs are of varying significance for each species' antimicrobial or innate immune response.¹²

Skin expression of AMPs has been demonstrated in humans¹³ and many animals, including primates,¹⁴ pigs,¹⁵ cows,¹⁴ sheep,¹⁶ chickens,¹⁷ rats,¹⁸ horses¹⁹ and dogs.¹² Cutaneous AMPs are constitutively present and further induced by infection or injury or both (Figure 1).⁴

In normal human skin, the main source of AMPs is the keratinocyte.²⁰ Synthesis of AMPs primarily occurs in the stratum granulosum; AMPs are then packaged into lamellar bodies and transported to the stratum corneum.²¹ Sebocytes, mast cells and neutrophils are also important sources of AMPs in normal human skin.²⁰ Antimicrobial peptides are also present in skin secretions, such as saliva and sweat.⁴

Upon skin infection or injury or both, recruited neutrophils, mast cells and other leukocytes contribute to the majority of AMP production.²⁰ Production is triggered by activation of pattern recognition receptors, such as Toll-like receptors (TLRs), mannose receptors and helicases.⁴ These receptors are activated by lipopolysaccharides from Gram-negative bacteria, lipoteichoic acid and peptidoglycans from Gram-positive bacteria, mannans from yeast and fungi, and nucleic acids from pathogens and self.^{4,22} Antimicrobial peptide upregulation is a secondary response, which limits the severity of infection or injury when the primary line of defense (constitutive AMP expression) fails.²⁰

A major role of AMPs in innate immunity is their direct antibiotic-like inhibition of microbial pathogens. Most

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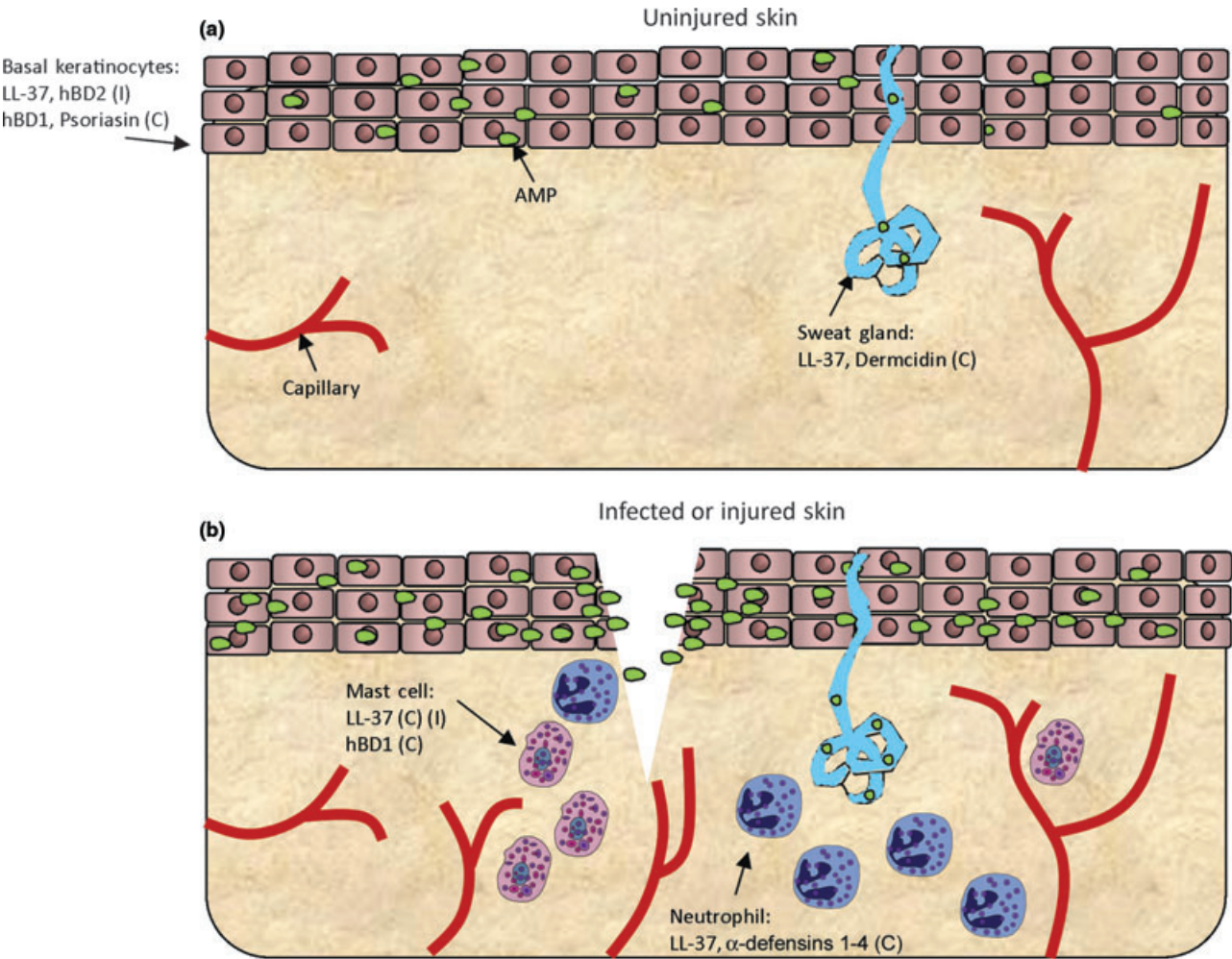


Figure 1. Antimicrobial peptide (AMP) expression in normal and infected or injured skin. (a) Normal skin is composed of an epidermal layer (keratinocytes) and a dermis containing capillaries. Keratinocytes and sweat glands produce low levels of AMPs to minimize microbial colonization. (b) Upon infection or injury, keratinocytes increase AMP production, which initiates neutrophil and mast cell recruitment to the site of injury via chemotaxis. These infiltrating leukocytes also make AMPs, and the consequent robust increase of AMPs at the injured site stimulates angiogenesis and keratinocyte proliferation to regenerate the damaged tissue. Abbreviations: C, constitutive expression; and I, inducible. (Adapted from Radek and Gallo,²⁶ with permission).

AMPs carry an overall net positive charge; this ensures their interaction with the negatively charged phospholipids in the cell membranes of both Gram-positive and Gram-negative bacteria, as well as the anionic components of fungi and viruses.^{23,24} The peptides attach to, align with, and then insert into the microbial phospholipid bilayer.²⁵ As the peptides associate with the lipid head groups of the phospholipid bilayer, transmembrane 'pores' form.^{25,26} The 'pores' disrupt and destabilize the bacterial cell membrane, ultimately leading to bacterial lysis.^{25,26} Antimicrobial peptides preferentially target replicating bacteria, especially at the site of cell division.²⁷

There are many AMPs expressed in human and animal skin. Together, they carry out a variety of functions in cutaneous host defense, ranging from influencing cell signalling to inhibiting the growth of a wide spectrum of pathogens. The expression, structures, processing, induction and antimicrobial and immunomodulatory properties vary between the peptides.¹⁹ Cathelicidins and β -defensins are the well-characterized AMPs.^{11,28,29} Key features of human cathelicidin and β -defensins are summarized in Table 1.

Table 1. Key features of human antimicrobial peptides (adapted from Izadpanah and Gallo,⁴⁰ with permission)

	Cathelicidins	β -Defensins
Structure	α -Helix Cathelin prodomain	β -Sheet Six cysteine motifs Disulfide bridges
Source	37 Amino-acid peptides, other processed forms Keratinocytes, neutrophils, mast cells, lymphocytes, sweat glands	Keratinocytes, sebocytes, sweat glands
Regulation	Constitutive and inducible	Constitutive and inducible
Antimicrobial properties	Broad spectrum	Broad spectrum

Cathelicidins

Cutaneous expression

Cathelicidins were the first AMPs found in mammalian skin.³⁰ Since their discovery, cathelicidins have been identified in the skin of humans,³¹ marsupials,³² dogs³³ and cats.³⁴

In humans, cathelicidin predominantly resides in granules of the superficial epidermis and in the extracellular spaces in the stratum corneum.³⁵ Likewise, in dogs, it resides in the stratum granulosum and less so in the stratum corneum.^{33,36}

Structure

Only one cathelicidin is encoded by humans (LL-37), mice (CRAMP) and dogs (cCath), while multiple cathelicidins have been discovered in pigs, horses, cattle and chickens.^{11,37}

The human cathelicidin gene (*CAMP*) encodes an 18 kDa α -helical precursor protein [human cathelicidin antimicrobial protein (hCAP-18)]⁴ that consists of an N-terminal prodomain region, cathelin, the amino-acid sequence of which is highly conserved across species.^{38–40} In contrast, the C-terminal domain of hCAP-18 varies between 20 and 40 amino acids among different species; this variability contributes significantly to the broad-spectrum antimicrobial activity of cathelicidins.²⁶ The hCAP-18 has a 68% mRNA sequence similarity and a 57% protein sequence similarity to cCath.³⁶

Peptide processing is essential for providing both the regulation and diverse biological activity of cathelicidin.²⁹ The full-length precursor, hCAP-18, is thought to be inactive in its immature form.²⁹ The hCAP-18 is commonly cleaved by serine proteases, such as kallikrein 5 and 7 in keratinocytes, and by neutrophil proteases, such as serine protease 3, to release the mature 37-amino-acid peptide that begins with two leucine residues, LL-37.^{37,41–43} In sweat, LL-37 is further processed, generating KR-20, a 20-amino-acid derivative, KS-30, a 30-amino-acid derivative, and RK-31, a 31-amino-acid derivative.^{44,45}

Unlike hCAP-18, processed cathelicidins demonstrate fast, potent, broad-spectrum antimicrobial activity.²⁶ The expression of cathelicidin as a full-length precursor that requires proteolysis for its activation allows for the stable control of its antimicrobial and proinflammatory action in the presence of particular stimuli.²⁶

Induction

Infection, cutaneous injury and vitamin D₃ are all potent inducers of cathelicidin expression. LL-37 is induced by both bacterial components, such as lipopolysaccharide, and proinflammatory mediators, such as interleukin-6 and retinoic acid.^{46,47} Cathelicidin expression levels are upregulated in the presence of Gram-positive bacteria.^{48,49} LL-37 is induced within the epidermis during the development of verruca vulgaris.⁵⁰ Cutaneous injury induces the release of cathelicidin active against group A *Streptococcus*.³¹ Vitamin D₃ can also induce hCAP-18/LL-37 expression in keratinocytes.⁴²

Antimicrobial functions

Cathelicidins are potent antimicrobial agents. Cathelicidins possess an intrinsic ability to kill Gram-negative and Gram-positive bacteria, fungi and viruses.^{44,46} Cathelicidin expression levels correlate with resistance to cutaneous infections.⁵¹ The CRAMP knockout mice show increased susceptibility to skin infections with group A *Streptococcus* and vaccinia.⁵² LL-37 has been shown to neutralize lipopolysaccharide endotoxin.⁵³

Immunomodulatory functions

Antimicrobial peptide LL-37 interacts with mammalian cells to induce a host response by triggering inflammatory cell recruitment and cytokine release (Figure 2). LL-37 acts as a chemoattractant through binding of formyl peptide receptor-like 1, which belongs to the G_i protein-coupled receptor family.⁵⁴ LL-37 promotes the recruitment of neutrophils, T cells, mast cells and monocytes to sites of injury and infection, and stimulates angiogenesis.^{54–56} LL-37 also induces histamine release from mast cells and intracellular Ca²⁺ mobilization.⁵⁷ Cathelicidin may help repair skin wounds by inducing keratinocyte migration via transactivation of the epidermal growth factor receptor.⁵⁸ LL-37 significantly inhibits the lipopolysaccharide-induced release of proinflammatory cytokines by macrophages.⁵⁹ LL-37 influences TLR signalling in immune cells, specifically by inhibiting TLR4- but not TLR2-mediated induction of dendritic cell maturation and cytokine release.⁶⁰ LL-37 also binds extracellular self-DNA fragments, enabling them to enter plasmacytoid dendritic cells, which initiates TLR9 activation to produce type I interferons.²⁸ LL-37 changes the expression of phagocytic receptors, significantly enhancing the ability of dendritic cells to undergo phagocytosis.⁶¹ The immunomodulatory mechanisms of cathelicidin complements its antimicrobial properties and reinforce its role as an integral defense molecule in innate immune responses.

β -Defensins

Cutaneous expression

β -Defensins (BDs) identified in mammalian skin include human BD (hBD) 1, 2 and 3, chicken gallinacin-3, bovine lingual AMP, porcine BD2, 3, 4 and 129, equine BD2 and canine BD (cBD) 1, 2, 3, 102, 103, 122 and 127.^{12,15,17,62–64} Of the cBDs, only cBD1 and cBD103 have readily detectable cutaneous expression, with cBD103 having the highest expression.⁶⁵ The cCath has a higher mRNA expression in canine skin than cBD1, 2 and 3, with a more than 358-fold expression compared with cBD2.³³ cCath mRNA expression level was followed by cBD3 and cBD1, while cBD2 was the least expressed.³³

Canine BD1, cBD2, cBD3 and cCath fluorescence show cytoplasmic expression.³³ Canine BD2 and cBD3 are diffusely distributed throughout the epidermis.^{33,36} Immunohistochemistry demonstrated cBD103 peptide in the epidermis, hair follicles and sebaceous glands comparable to hBD3 expression in human skin.⁶² Equine BD2 was detected in the apocrine glands of the equine scrotal skin.⁶³ Skin specimens from the ventrum and dorsum of six dogs of different breeds and ages showed essentially the same cBD103 mRNA expression level when comparing skin from the different dogs, and also when comparing the dorsal or ventral surface.⁶⁵

Structure

Defensins are low molecular weight (3–5 kDa) AMPs.^{10,66} They have arginine residues and six conserved cysteine residues that form intramolecular disulfide bridges, which stabilize their triple-stranded β -sheet structure.⁴ A major defensin family produced in the skin is the BD.⁴

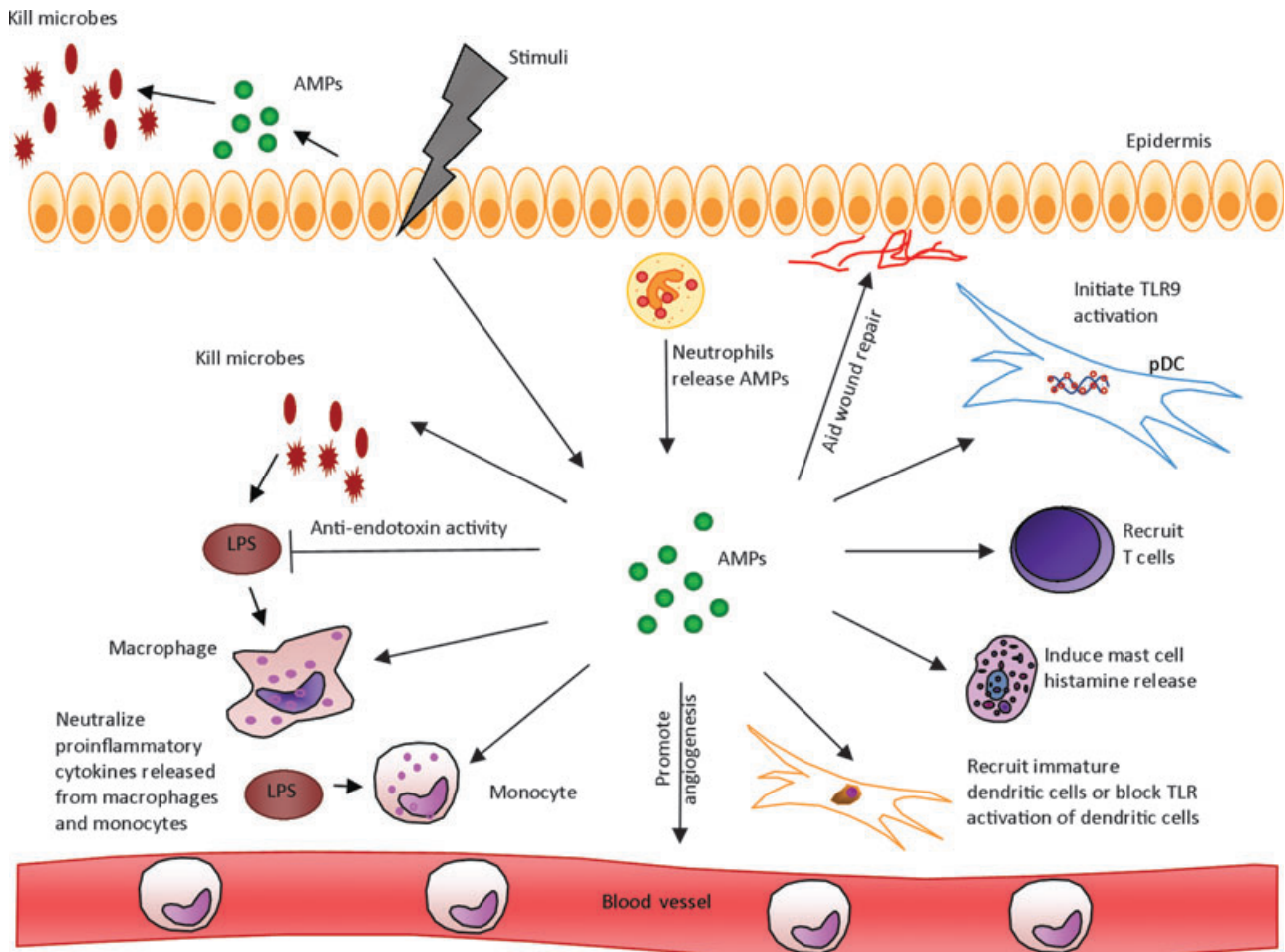


Figure 2. Several of the functions of AMPs in host defense. Antimicrobial peptides recruit leukocytes to the infection site, block or activate TLR signalling, protect against infection, control inflammation and promote wound healing. Abbreviations: AMP, antimicrobial peptide; LPS, lipopolysaccharide; pDC, plasmacytoid dendritic cell; and TLR, Toll-like receptor (Adapted from Lai and Gallo,²⁸ with permission).

Human BDs have a homology of about 51–71% with the first three cBDs.⁶⁷ Based on sequence comparisons, it appears that cBD1 is an orthologue of hBD1, cBD103 of hBD3, and that cBD102 and hBD2 have no equivalent orthologues.⁶⁵ The gene encoding cBD103 demonstrates two polymorphisms: a common 3 bp deletion allele and a gene copy-number variation.⁶⁵ Golden retriever and Labrador retriever dogs encode the variant cBD103 allele, cBD103ΔG23, and the cBD103 gene copy-number polymorphism.⁶⁵

Induction

β-Defensins are produced by keratinocytes, sebocytes and sweat glands.⁶⁸ Keratinocytes constitutively express hBD1.⁴ Keratinocyte hBD2, 3 and 4 expression levels are very low at the steady state and typically are upregulated by infection, proinflammatory cytokines (e.g. tumour necrosis factor-α, interferon-γ) and injury; they then accumulate in the skin.^{69–72} *Staphylococcus epidermidis*, a skin commensal bacterium, upregulates hBD2 and hBD3 expression via TLR2-induced p38 mitogen-activated protein kinase signalling.⁷³ Chronic wounds have a higher baseline expression of hBD2, probably maintained by ongoing tissue damage and bacterial exposure.⁷⁴ Middle- to long-chain sebum free fatty acids lauric acid, palmitic acid and oleic acid enhance the innate immune

defense of the skin by inducing hBD2 in human sebocytes.⁷⁵

Antimicrobial functions

Human BD1 exhibits minor antimicrobial activity compared with other defensins.^{76,77} While hBD1 and hBD2 demonstrate strong activity against Gram-negative bacteria, such as *Escherichia coli* and *Pseudomonas aeruginosa*, neither is particularly active against Gram-positive bacteria, including *Staphylococcus aureus*.⁶⁹ Human BD3, however, has broad-spectrum activity against Gram-negative and Gram-positive bacteria, particularly *S. aureus*, and fungi.^{78,79}

The activity of β-defensins against infections has also been studied in canine skin. Recombinant cBD103 and cBD103ΔG23 exhibited potent and similar antimicrobial killing of both meticillin-susceptible and meticillin-resistant *Staphylococcus pseudintermedius*.⁶⁵ Both sets of canine BDs showed potent antimicrobial activity against endogenous bacteria found on canine skin (*Bacillus licheniformis*, *Micrococcus* spp. and *Bacillus cereus*), in addition to a laboratory strain of *Escherichia coli* D31.⁶⁵

Immunomodulatory functions

In addition to antimicrobial defense, BDs also exhibit diverse immunomodulatory roles (Figure 2). hBD2

promotes histamine secretion from mast cells, suggesting a role for hBD2 in the allergic pathway.⁸⁰ Human BD2 is chemotactic for immature dendritic cells and memory T cells.⁸¹ Human BD2, hBD3 and hBD4 stimulate keratinocytes to increase their gene expression of many proinflammatory cytokines, chemokines and proteins, including interleukin-6, interleukin-10, monocyte chemoattractant protein-1 and macrophage chemoattractant protein-1.⁸² Human BDs also elicit intracellular Ca^{2+} mobilization and participate in wound repair by increasing keratinocyte migration and proliferation.⁸² Of note, a mutation of a BD in dogs has been associated with coat colour.⁸³ This observation underscores the pleiotropic and sometimes unexpected functions of AMPs.

Dermcidin

The AMP dermcidin is constitutively expressed as a small precursor protein in eccrine sweat glands.⁸⁴ Dermcidin is secreted into sweat, where it is activated through proteolysis.⁸⁴ In contrast to most AMPs, dermcidin-derived AMPs do not induce pore formation on the bacterial cell membrane;⁸⁵ however, they do bind to unidentified targets on the bacterial cell envelope, leading to decreased RNA and protein synthesis.⁸⁵ Dermcidin exhibits antimicrobial activity against *S. aureus*, *E. coli* and *Candida albicans*.⁸⁴

Psoriasin

Psoriasin is an AMP in the skin of humans, cows and horses.^{19,86} It is the most hydrophobic epidermal AMP.⁸⁷ Psoriasin may be secreted with sebum lipids; large amounts accumulate in sebaceous glands and the epidermis of sebaceous skin.⁸⁷ Psoriasin expression is upregulated in keratinocytes *in vivo* and *in vitro* after *E. coli* challenge.⁸⁷

Antimicrobial peptide production in atopic dermatitis

Atopic dermatitis, an inflammatory pruritic skin disease, occurs in humans, horses,⁸⁸ cats⁸⁹ and dogs.⁹⁰ Canine atopic dermatitis, which affects approximately 10% of all dogs, has an immunopathogenesis comparable to that of human atopic dermatitis.⁶² Similar to their human atopic counterparts, who have high rates of secondary recurrent *S. aureus* and *Malassezia* spp. infections,⁹¹ there are high rates of *S. pseudintermedius* and *M. pachydermatis* superinfections in canine atopic skin.⁹⁰ These cutaneous superinfections complicate management and further compromise the integrity of the skin barrier, and may be due in part to abnormally low AMP levels.

In humans, atopic dermatitis skin has significantly lower AMP expression than psoriatic skin, even though both disorders are associated with inflammation and a defective cutaneous barrier.⁵¹ This defect has been attributed to AMP suppression by elevated levels of T-helper 2 cytokines interleukin-4 and interleukin-13 in atopic dermatitis.^{69,70} Lower AMP levels create a diminished antimicrobial barrier, and consequently, an increased susceptibility to *S. aureus* and other microbial superinfec-

tions in atopic dermatitis patients.^{51,92,93} A history of eczema herpeticum is associated with the inability to induce hBD2, hBD3 and cathelicidin in the skin of patients with atopic dermatitis.⁹⁴ A hBD1 polymorphism is associated with the atopic dermatitis phenotype.⁹⁵

The expression levels of cBD1, cBD2, cBD3 and cCath are increased in canine lesional and nonlesional atopic skin compared with the skin of healthy dogs.^{36,62} Canine lesional skin cBD1 expression was 12-fold higher, and nonlesional skin cBD1 expression fivefold higher, than cBD1 expression in the skin of healthy control dogs.⁶² No comparison between expression in atopic lesional skin and lesional skin of normal dogs with inflammation by scratch or wound injury was made; therefore, it is unclear whether the atopic milieu also suppressed induction of these AMPs in dogs. Furthermore, data on cBD103 expression are conflicting. Expression of cBD103 has been found to be both twofold downregulated⁶² and similar⁶⁵ in atopic dogs compared with healthy dogs. Expression of cBD103 was comparable at lesional and nonlesional sites.⁶⁵ The increased cBD1, cBD2, cBD3 and cCath expression and similar or decreased cBD103 expression in the skin of atopic dogs suggests that their canine cutaneous innate immune system may be altered.^{36,62} Whether this partly explains the recurrent secondary bacterial infections in dogs with atopic dermatitis requires additional study. The investigation of the involvement of AMPs in the pathogenesis of atopic dermatitis in animals is complicated by multiple confounding factors, such as different breeds, living conditions and diet.³⁶ The functional role of AMPs in atopic dermatitis, especially with regard to susceptibility to recurrent superinfections, requires further analysis.

Conclusion

Antimicrobial peptides constitute an evolutionarily conserved defense system that is an important component of cutaneous innate immunity. These peptides have antimicrobial and immunomodulatory effects, many of which have only recently been defined, and which influence both the immediate defense response and the slower adaptive and repair processes. As these peptides continue to be investigated, their precise function and relevance in skin and its pathology will be better defined. The multiple roles of AMPs as 'natural antibiotics' and 'immune regulators' suggest that they may be promising therapeutic agents. Thus, a greater understanding of the protective properties of AMPs yields great promise for new strategies in the control of cutaneous disease.

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Résumé

Contexte – Les peptides antimicrobiens (AMPs) ont un rôle crucial dans l'immunité cutanée innée. Ils sont présents dans la peau de nombreux animaux, dont celle des mammifères, et sont à la fois présents constitutivement ou induits pas une infection ou une blessure.

Fonctions – Les peptides antimicrobiens présentent une activité antimicrobienne contre bactéries, virus, champignons et parasites avec différentes puissances dépendantes de leur structure peptidique. Ils agissent aussi comme molécules effectrices multifonctionnelles qui influencent divers processus cellulaires, comme la migration cellulaire, la prolifération et la différenciation, la production de cytokine, l'angiogénèse et la cicatrisation. La suppression de la production d'AMP a été associée à une augmentation de sensibilité aux microbes et à la pathogénie de la dermatite atopique.

Cette revue appuie sur les récentes observations de l'expression et du rôle des AMPs, particulièrement la cathélicidine et la β -défensine dans la peau saine et malade.

Resumen

Introducción – los péptidos antimicrobianos (AMPs) tienen un papel crucial en la inmunidad natural cutánea. Están presentes en la piel de muchos animales, incluyendo mamíferos, y están tanto presentes constitutivamente como son inducibles por infecciones y lesiones.

Funciones – los péptidos antimicrobianos desarrollan actividad antimicrobiana frente a bacterias, virus, hongos y parásitos, con diversa potencia dependiendo de su estructura peptídica. También actúan como moléculas efectoras multifuncionales que influyen en procesos celulares diversos, incluyendo migración celular, proliferación y diferenciación, producción de citoquinas, angiogenesis y cicatrización de heridas. Una reducción en la producción de AMPs se ha asociado con susceptibilidad creciente a insultos microbianos y con la patogenia de la dermatitis atópica.

Esta revisión destaca observaciones recientes respecto a la expresión y al papel de los AMPs, particularmente la catelicidina y la β -defensina, en piel sana y enferma.

Zusammenfassung

Hintergrund – Antimikrobielle Peptide (AMPs) spielen eine entscheidende Rolle bei der angeborenen kutanen Immunität. Sie sind in der Haut vieler Tiere, so auch bei den Säugetieren vorhanden, wobei sie sowohl grundsätzlich präsent als auch durch Infektion und Verletzung induzierbar sind.

Funktionen – Antimikrobielle Peptide zeigen eine antimikrobielle Wirksamkeit gegenüber Bakterien, Viren, Pilzen und Parasiten, wobei die unterschiedliche Wirkung auf ihrer Peptidstruktur beruht. Sie wirken auch als multifunktionelle Effektormoleküle, die die diversen zellulären Prozesse beeinflussen. Davon betroffen sind die Zellmigration, Proliferation und Differenzierung, Zytokinproduktion, Angiogenese und Wundheilung. Eine unterdrückte AMP Produktion wird mit zunehmender Empfindlichkeit auf mikrobielle Insulte und der Pathogenese der atopischen Dermatitis in Zusammenhang gebracht.

Diese Review unterstreicht jüngste Beobachtungen bei der Expressierung und der Rolle von AMPs, vor allem der AMPs Cathelicidin und β -Defensin, in gesunder und erkrankter Haut.

要約

背景–抗菌ペプチド（AMPs）は皮膚の自然免疫として重要な役割をもっている。それらは哺乳類を含む多くの動物の皮膚に認められ、恒常的に存在して感染や損傷により誘導される。

機能–抗菌ペプチドは細菌、ウイルス、真菌、寄生虫に対して抗菌活性を示し、それらのペプチドの構造によって異なった性質を示す。また細胞の移動、増殖、分化、サイトカイン産生、血管新生、創傷治癒などの様々な細胞の過程に影響する多機能性のエフェクター分子として働く。AMPsの産生が抑制されると細菌に対する傷害性が増加に関連し、アトピー性皮膚炎の病因にも関係する。

この総説は近年のAMPs発現と役割に関する見解を、健康なおよび疾患の皮膚でAMPsでのカセリシジンと β ディフェンシンを中心にして述べる。

摘要

背景 – 抗菌肽（AMPs）在皮肤先天性免疫中至关重要。它们存在于许多动物的皮肤上，包括哺乳动物，既是皮肤基本构成也能被感染和损伤诱导产生。

功能 – 抗菌肽表现出对细菌、病毒、真菌和寄生虫的抗微生物活性，不同的功效取决于它们的缩氨酸（肽）结构。它们还充当多功能的效应分子，影响不同的细胞过程，包括细胞移动、增殖和分化、细胞因子生成、血管生成和伤口愈合。抑制AMP产物会提高机体对微生物损伤的敏感性，增加异位性皮炎的发病。

本综述展示了在近期研究中，健康和疾病皮肤的AMPs表达和作用，特别是卡特兰杀菌素和 β -防御素AMPs。