Received: 19 December 2022 | Accepted: 26 October 2023

DOI: 10.1111/vde.13215

Veterinary Dermatology

REVIEW

# Update on the skin barrier, cutaneous microbiome and host defence peptides in canine atopic dermatitis

**Domenico Santoro**[1] | **Manolis Saridomichelakis**[2] | **Melissa Eisenschenk**[3] | **Chie Tamamoto-Mochizuki**[4] | **Patrick Hensel**[5] | **Cherie Pucheu-Haston**[6] | **for the International Committee on Allergic Diseases of Animals (ICADA)**[†]

[1]Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, Florida, USA

[2]Clinic of Medicine, Faculty of Veterinary Science, University of Thessaly, Volos, Greece

[3]Pet Dermatology Clinic, Maple Grove, Minnesota, USA

[4]Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, North Carolina, USA

[5]Tierdermatologie Basel, Münchenstein, Switzerland

[6]Department of Veterinary Clinical Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge, Louisiana, USA

**Correspondence**
Domenico Santoro, Department of Small Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, Florida, 32610, USA.
Email: dsantoro@ufl.edu

## Abstract

**Background:** Canine atopic dermatitis (AD) is a complex inflammatory skin disease associated with cutaneous microbiome, immunological and skin barrier alterations. This review summarises the current evidence on skin barrier defects and on cutaneous microbiome dysfunction in canine AD.

**Objective:** To this aim, online citation databases, abstracts and proceedings from international meetings on skin barrier and cutaneous microbiome published between 2015 and 2023 were reviewed.

**Results:** Since the last update on the pathogenesis of canine AD, published by the International Committee on Allergic Diseases of Animals in 2015, 49 articles have been published on skin barrier function, cutaneous/aural innate immunity and the cutaneous/aural microbiome in atopic dogs. Skin barrier dysfunction and cutaneous microbial dysbiosis are essential players in the pathogenesis of canine AD. It is still unclear if such alterations are primary or secondary to cutaneous inflammation, although some evidence supports their primary involvement in the pathogenesis of canine AD.

**Conclusion and Clinical Relevance:** Although many studies have been published since 2015, the understanding of the cutaneous host–microbe interaction is still unclear, as is the role that cutaneous dysbiosis plays in the development and/or worsening of canine AD. More studies are needed aiming to design new therapeutic approaches to restore the skin barrier, to increase and optimise the cutaneous natural defences, and to rebalance the cutaneous microbiome.

**KEYWORDS**
ceramides, cutaneous dysbiosis, filaggrin, host defence peptides

## INTRODUCTION

Canine atopic dermatitis (AD) is a hereditary, generally pruritic and predominantly T-cell-driven inflammatory skin disease involving interplay between skin barrier abnormalities, allergen sensitisation and microbial dysbiosis. In 2015, the International Committee on Allergic Diseases of Animals (ICADA) published a series of articles highlighting the most up-to-date information on the pathogenesis of AD. Since then, many articles have been published on the skin barrier structure, innate immunity and cutaneous and aural microbiome alterations in atopic dogs. These publications are reviewed in this article along with a brief review of the previous literature on these topics. For more detailed information on the previous literature, the reader should refer to the ICADA pathogenesis articles published in 2015.

Alterations of the skin barrier function are attracting significant interest in veterinary and human dermatology. In the previous edition of this review series, published in 2015,[1] it was made clear that skin barrier dysfunction, along with immunological alterations,

[†]The International Committee on Allergic Diseases of Animals (ICADA) members presented in Acknowledgements section.

represent the core of the pathogenesis of canine AD. Whether skin barrier dysfunction is a primary defect and/or appears secondarily to cutaneous inflammation was, and still is, open to debate. Since that publication, more research has been published on the differences between atopic and healthy canine skin suggesting some primary defects of the barrier, at least in some dogs with AD. Unfortunately, very few studies have compared skin barrier function between AD and other inflammatory, nonallergic skin conditions to determine if these alterations are intrinsic to canine AD or instead the result of a nonspecific cutaneous inflammatory response.

The aim of this review was to report updates from research published on skin barrier integrity, host–microbe interaction, as well as the cutaneous and aural microbiome in dogs with AD.

## METHODS AND MATERIALS

A literature search for studies on canine AD published between 2015 and 2023 was conducted using PubMed (pubmed.gov), Web of Science (Thomson Reuters), CAB Abstracts (EBSCOhost Research Databases) and CAB Abstracts Archive (EBSCOhost Research Databases). Restrictions (date or language) were not enforced for the article search. Published abstracts from the annual meetings of the European Society of Veterinary Dermatology/European College of Veterinary Dermatology, American Academy of Veterinary Dermatology/ American College of Veterinary Dermatology and the World Congresses of Veterinary Dermatology between 2015 and 2023 were included. A total of 49 articles were selected and summarised below.

## UPDATES ON SKIN BARRIER EVALUATION

Most research on skin barrier function in dogs has been performed using indirect measures of skin integrity (e.g. trans epidermal water loss [TEWL]), or assessing the epidermal ceramide content or the presence of filaggrin in atopic skin.[1] The TEWL has been the parameter most commonly used to indirectly and atraumatically assess the functionality of the skin barrier. However, this methodology has significant limitations being affected by multiple environmental factors (e.g. room temperature and humidity) as per manufacturers' indications. Recently, it has been demonstrated that some TEWL instruments have high inter- and intraobserver variability (VapoMeter; Delfin Technologies Ltd).[2] Such instruments also may not be able to detect alterations in mildly affected dogs, and the reported values may not correlate with the severity of clinical signs in subsets of dogs with AD.[2] Larger studies using accurate and precise instruments are needed to verify the results reported previously.

Since the last series of ICADA updates on the pathogenesis of canine AD, no methodologies able to directly assess the skin barrier integrity have been optimised in either humans or in dogs. TEWL assessment remains the most widely used method. Owing to the variability of this methodology, other techniques have been investigated. A pilot study showed that the use of the Corneometer (Courage+Khazaka electronic GmbH) to assess skin hydration and of the pH meter (Courage+Khazaka electronic GmbH) for the measurement of the cutaneous pH had more reliable results with a lower inter- and intraobserver variability compared to the VapoMeter (Delfin Technologies Ltd).[2] In the same study, the authors showed that the Colorimeter (Courage+Khazaka electronic GmbH), to assess the degree of erythema and the pH meter were able to detect significant differences in nonlesional atopic skin when compared to healthy skin.[2] These results may suggest a lower sensitivity for the VapoMeter when compared to the other instruments.[2] Because of increased sensitivity and reliability of newer instruments, the concurrent assessment of cutaneous pH, hydration, erythema and TEWL versus just the evaluation of TEWL alone has been the preferred noninvasive approach to assess skin barrier integrity in dogs. Using these methods, newer studies tried to correlate the degree of skin barrier dysfunction with the clinical severity of AD. A recent study[3] assessed the skin microbiome and cutaneous barrier integrity in atopic dogs during and after a flare. The authors showed that the TEWL (as measured with a TEWA-meter; Courage+Khazaka electronic GmbH) positively correlated with the clinical severity of the disease,[3] while there was a negative correlation between pH (via the pH meter) and severity of the clinical signs.[3]

Altogether, these studies indicate that currently the assessment of TEWL, skin hydration and pH are the most frequently used atraumatic tools to evaluate the integrity of the skin barrier in atopic dogs. More studies evaluating alternative methodologies, such as tape-stripping analysis,[4] may be warranted for a better evaluation of the skin barrier function.

## UPDATES ON STRATUM CORNEUM LIPIDS

Keratinocytes, representing the major cell type forming the epidermis, are embedded in the cement of a well-organised lipid layer that covers each corneocyte and functions as a seal between cells. As part of the lipid component of the skin barrier, ceramides have been intensively investigated over the years. Their amount, spatial organisation and diversity are essential for the integrity of the skin barrier. Most of the studies on ceramides were done in the first decade of the twenty-first century. These studies showed that, in both humans and dogs, a significant reduction in ceramide amount and/or types is present in lesional and nonlesional skin of atopic patients when compared to healthy skin.[1,5–7] Such reduction in ceramide composition has been attributed, in part, to the inflammatory response triggered by allergen exposure in sensitised individuals. The ceramides most frequently found to be altered in AD, when compared to healthy controls,

include ceramide 1/CER[EOS], ceramide 9/CER[EOP] and ceramide CER[NP].[1,7,8] These findings were demonstrated in both experimentally sensitised[5] and naturally affected[5] atopic dogs.

A recent small study in 2018[9] which investigated the relative abundance of each ceramide, the total lipid content and the stratum corneum (SC) organisation in healthy and atopic dogs challenged previous results. In particular, the authors showed that the SC of atopic dogs is characterised by a hexagonal lipid packing instead of the classic orthorhombic packing characterising the lamellar organisation of lipids in healthy skin.[9] This alteration was accompanied by a decrease in the relative abundance of free fatty acids (and not of ceramides or cholesterol) in atopic compared to healthy skin.[9] Neither relative abundance of several ceramide subclasses nor total ceramide content differed between atopic and healthy skin. However, a decreased ratio of CER[NS] C44/C34 was seen in atopic skin.[9] The ratio of CER[NS] C44/C34 showed a nonlinear negative correlation with the clinical severity of AD.[9]

In summary, not many new studies have been published evaluating the ceramide composition in the SC of atopic dogs. However, although small in size (only three healthy and five atopic dogs were included), the study by Chermprapai et al.[9] opened a new perspective on the potential involvement of lipid disturbances in the pathogenesis of canine AD. The importance of this study resides in the concept that the spatial organisation and carbon atom composition of ceramide may be as important as the amount of ceramides present in the SC of atopic skin.

## UPDATES ON STRATUM CORNEUM STRUCTURAL PROTEINS

Along with lipids, structural proteins such as filaggrin, filaggrin 2, involucrin and corneodesmosin are essential for the formation of the cornified envelope. Filaggrin has attracted much attention in the past two decades for its role in human AD. In people, while not present in all patients, filaggrin gene mutations have been recognised as one of the most reliable genetic factors predisposing to the development of AD.[10] In a subset of dogs with AD, a decrease in or an undetectable expression of epidermal filaggrin has been demonstrated via immunofluorescence.[11] Mutations of the filaggrin gene have not been associated with canine AD in most of the breeds in which this gene has been evaluated. However, a single-nucleotide polymorphism in the filaggrin gene was strongly associated with AD in Labrador retrievers from the UK, suggesting the potential role of filaggrin in specific breeds and geographical locations.[12] Such findings may help explain breed-specific phenotypes in canine AD.[13] Because of these contrasting data, although filaggrin is recognised as an important component of the skin barrier, its involvement in the pathogenesis of AD remains unknown.

In recent years, investigation of the canine filaggrin structure has resulted in the identification of a very similar S100 fused-type protein, called filaggrin 2.[14,15] Filaggrin 2, like filaggrin, is involved in the production of natural moisturising factors (NMFs), and also is an integral component of the cornified envelope.[16-18] Because of the poor characterisation of canine filaggrin, it is likely that some of the older studies suggesting an alteration of filaggrin expression in atopic skin were actually investigating filaggrin 2 rather than filaggrin.[17,18] Controversial results have been published after 2015 on the expression of the enzymes involved in the degradation of filaggrin in atopic dogs.[19,20] One immunohistochemical study showed decreased caspase-14 in the nonlesional skin of atopic dogs when compared to healthy dogs,[19] while another study showed increased expression of calpain-1, caspase-14 and matriptase in nonlesional skin of atopic dogs compared to healthy breed-matched dogs.[20]

Thus, current data on the involvement of filaggrin and filaggrin 2 in the pathogenesis of canine AD remain controversial. It is still unknown if the demonstrated alterations of these proteins, enzymes and NMFs represent a primary defect or are secondary to an inflammatory state. A very recent study, using experimentally sensitised atopic dogs,[21] indirectly suggested that some of these alterations may be a result of cutaneous allergic inflammation rather than being a primary defect.

Along with filaggrins and NMFs, other structural proteins that have been studied in atopic dogs and humans include the tight junction proteins claudin-1 and occludin.[22–25] Both proteins have been shown to be significantly decreased in the skin of atopic dogs when compared to healthy canine skin, further highlighting the impaired skin barrier in dogs with AD. Recently,[22] using an experimental model of acute canine AD, authors have shown a decrease in protein expression and distribution of corneodesmosin, another structural protein present in the SC, in atopic skin when compared to healthy skin. The authors were able to demonstrate that, of five structural proteins examined (E-cadherin, desmocollin-1, desmoglein-1, corneodesmosin and claudin-1), the immunoreactivity of both corneodesmosin and claudin-1 was heterogenous and of reduced intensity after a single house dust mite (HDM) epicutaneous challenge.[22]

In summary, much is still left to learn about the involvement of structural proteins in the pathogenesis of canine AD. Filaggrin is the most extensively studied structural protein associated with both human and canine AD. However, other studies have demonstrated the involvement of additional structural components of the SC (and viable epidermis) in the alteration of the skin barrier in AD. Of particular interest are alterations of the tight junctions and corneodesmosomes. More recently, in human AD, the involvement of other junctional structures, such as the gap and adherens junctions, has been proposed as another cause of disrupted skin barrier in AD.[26] Such studies point to more complex structural changes of the skin barrier in AD that go beyond filaggrin and ceramides and warrant a more in-depth investigation.

## UPDATES ON CUTANEOUS MICROBIOME

Mammalian skin is covered by micro-organisms (bacteria, fungi, parasites and archaeans) that play a significant

role in the maintenance and integrity of the skin barrier, as well as constantly interacting with the local immune system.[27] As part of the cutaneous barrier, the skin microbiome and its alterations (cutaneous dysbiosis, defined as an imbalance in the composition of microbial population associated with reduction in microbial diversity and in the number of beneficial bacteria)[27] have been of central interest in the past decades. Multiple studies have demonstrated that both dogs and humans with AD suffer from cutaneous dysbiosis.[1,27–34] Whether the dysbiosis is a cause or a consequence of the atopic state remains unclear. However, a recent birth cohort study sampling 109 puppies and 34 parent dogs from Switzerland showed that although the development of skin microbiota (bacterial and fungal) is influenced by both age and environmental factors (e.g. level of hygiene), it is not associated with the development of AD.[31] At the time of the previous edition of this article series,[1] very little was known about cutaneous dysbiosis in dogs with AD. The most common finding was that a decrease in bacterial diversity is present in atopic canine skin[35] when compared with healthy skin. This decreased diversity favours the insurgence and relative predominance of *Staphylococcus pseudintermedius* above other organisms, with the potential for development of skin infections.

In the past decade, the cutaneous and gastrointestinal microbiome has been intensively studied; thanks to the widespread availability of technology capable of performing high-throughput sequence analysis.[30,33,36] With the advent of next-generation sequencing (NGS) technology, publications on the microbiome (mainly bacterial and fungal) in both dermatological and non-dermatological conditions of humans and animals have exponentially increased. In veterinary dermatology, studies have been mainly focused on canine AD.[27–34]

Previous studies have shown that the cutaneous microbiome in healthy dogs is highly diverse.[1,36] In the course of AD, the microbial diversity is significantly reduced in favour of staphylococcal organisms, leading to cutaneous dysbiosis.[1,36] The significant increase in the relative abundance of *S. pseudintermedius* in AD-associated pyoderma also was shown in a very recent study,[37] in which samples were collected from atopic dogs with active bacterial folliculitis. The microbiome analysis showed a significant reduction in microbial diversity in favour of *S. pseudintermedius* in both pustules and epidermal collarettes.[35] However, the other bacterial components of the 'normal' microbiota were still present, albeit in much reduced numbers.[37]

The body of literature on canine cutaneous microbiome has significantly increased in the past 5–10 years, yet most of the published data in canines are still more descriptive than mechanistic in nature. Efforts to clarify the role of microbiome in AD have used both experimentally[32] and naturally sensitised[27–31,33,34] atopic dogs. Overall, published studies suggest that dogs with AD have lower relative diversity in bacterial[36,37] and fungal[34,38,39] populations than do healthy dogs. An increased relative abundance of *S. pseudintermedius*[34,37] and *Malassezia pachydermatis*[34,39] has been reported on the skin of atopic dogs when compared to healthy dogs. Similar results were found in a recent study using an experimental model for canine AD.[32] In this study, the authors experimentally sensitised 14-month-old Beagle dogs ($n=6$) to *Dermatophagoides farinae* for 12 weeks. At the end of the sensitisation period, relative abundances of Firmicutes followed by Proteobacteria, Actinobacteria, Bacteroidetes and Tenericutes were detected. However, because it was outside of the scope of work, the authors did not assess any correlation between bacterial dysbiosis and development of clinical signs[30] or immunological alterations developing in this model.

The temporal changes of the cutaneous bacterial and fungal microbiota of dogs with AD were assessed in two recent studies.[39,40] Meason-Smith et al.[39] assessed the temporal changes in the cutaneous mycobiota of naturally and allergen-induced AD under certain circumstances (e.g. exposure to HDM).[39] Although a change in *Malassezia* population was not found in atopic dogs exposed to HDM, a difference in *Malassezia* spp. was seen between atopic (predominance of *M. pachydermatis*) and healthy (predominance of *M. globosa*) dogs.[39] Similar findings were reported in another study, by the same group of researchers, assessing temporal changes of the cutaneous bacterial community using atopic dogs experimentally sensitised and challenged with HDM.[40] The authors showed no changes in bacterial richness or diversity during the challenge; yet, there was an increase in the relative abundance of Corynebacteriaceae and Staphylococcaceae in the lesional skin which persisted for two weeks after the remission of skin lesions.[40]

To date, studies have not been able to determine the exact role of the cutaneous microbiome and its dysbiosis in the pathogenesis of AD, yet it is clear that the alterations of bacterial diversity correlate with skin barrier dysfunction, as measured by TEWL and pH.[3] It also is clear that the loss of cutaneous microbiome diversity is strongly associated with the presence of pyoderma in atopic dogs. In fact, another longitudinal study[3] using privately owned atopic dogs showed that the skin microbiome diversity significantly increased immediately after resolution of a flare and/or of a bacterial infection, becoming more like that of healthy skin. However, by 4–6 weeks post-treatment, the diversity had slowly decreased to become, once again, significantly lower when compared to healthy skin.[3] This decrease in microbiome diversity strongly correlated with the increase in relative abundance of *S. pseudintermedius*, which also correlated with the severity of the clinical signs of AD.[3]

## UPDATES ON AURAL MICROBIOME

Recently, greater interest has been devoted to aural microbiome and how its dysbiosis relates to canine AD.[34,41,42] The results of these studies showed that, in a similar way to the skin, a dysbiosis characterised by a lower species diversity also is present in the external ear canals of dogs with AD. However, as for the skin, is not known if such dysbiosis predisposes

atopic dogs to develop otitis. In a recent comparative study, a significant difference was found in the microbiome of the external ear canal in healthy ($n=9$) and atopic ($n=11$) dogs without signs of otitis externa.[41] The latter had a significantly higher relative abundance of *Staphylococcus* spp. (Firmicutes) and of *Ralstonia* spp. (Proteobacteria) organisms.[41] By contrast, a higher relative abundance of *Escherichia* spp. organisms was found in healthy compared to atopic ears.[41] Although the relative abundance of Firmicutes has been repeatedly found to be altered, this is the first study showing an alteration in the proteobacterium *Ralstonia* spp. *Ralstonia* is widely recognised to be an environmental organism, and for this reason, more studies are needed confirming its relevance in canine AD.

A second study from Europe confirmed the results reported by Ngo et al.,[41] by simultaneously assessing the aural and cutaneous microbiome of atopic without skin infection ($n=12$) and healthy ($n=12$) German shepherd dogs.[43] In this study, Apostolopoulos et al.[42] sampled multiple body regions (left axilla, left front dorsal interdigital region, left side of the groin and left external ear canal). After performing NGS, the authors were able to show no difference in bacterial diversity among the different body sites of healthy dogs. In these dogs, the most abundant bacterial phyla, in descending order, included Actinobacteria, Proteobacteria, Firmicutes and Bacteroidetes.[42] In atopic dogs, there also was no difference in bacterial diversity among body sites with the most abundant organisms belonging to the phyla Proteobacteria and Actinobacteria, followed by Firmicutes and Bacteroides.[42] Finally, when the microbiome of atopic dogs was compared to the microbiome of healthy dogs, there was no difference in bacterial diversity, although bacterial community richness of the former was lower in the axillary region.[42] The authors concluded that atopic German shepherd dogs have a different bacterial community composition and a lower diversity when compared to healthy dogs of the same breed.

In 2020, Tang et al. confirmed the results previously reported for both skin and ear microbiome, using a cohort of 172 healthy and 160 'clinically affected' dogs.[34] In that study, the authors defined as 'clinically affected' dogs with AD, with 'skin allergies', with nonhealing wounds, with wounds with and without biofilm formation, with pustules/ulcers/erosions or with other not precisely defined skin infections. At the end of the study, the researchers showed a significantly different bacterial microbiome on the skin of 'clinically affected' dogs with 16 bacterial species being relatively more abundant compared with healthy skin. The most abundant bacteria and fungi present on the skin of healthy dogs included *Cutibacterium acnes*, *S. pseudintermedius*, *Porphyromonas cangingivalis*, *Capnodiales*, unclassified fungal species and *Alternaria* sp. The most abundant species present on the skin of 'clinically affected' dogs included *S. pseudintermedius* and *S. schleiferi*. *Bacteroides pyogenes* and *Peptoniphilus grossensis* also were significantly more abundant in 'clinically affected' dogs than healthy dogs. As far the aural microbiome, 19 bacterial species and *M. pachydermatis* were relatively more abundant in the ears of 'clinically affected' dogs than healthy dogs. The top three most dominant bacteria in healthy ear samples included *C. acnes*, *S. pseudintermedius*, *Streptococcus* sp. and the top three most dominant fungi included *M. pachydermatis*, *Capnodiales* and *Pleosporales*. The most common organisms isolated from the ears of 'clinically affected' dogs included *M. pachydermatis*, *S. pseudintermedius*, *S. schleiferi* and a few anaerobic bacteria such as *Finegoldia magna*, *Peptostreptococcus canis* and *P. cangingivalis*.

## THERAPY AND CUTANEOUS MICROBIOME

Finally, two studies evaluated the effect of topical antimicrobial therapy[28] and phototherapy[29] on the cutaneous microbiome of dogs with AD. The first study was a very small pilot study assessing the microbiome in three atopic and three healthy dogs over 11 weeks. Dogs were sampled four weeks before (Day 0), then bathed twice weekly with a chlorhexidine-miconazole containing shampoo (Malaseb shampoo; Dermcare-vet Pty Ltd) for three weeks (weeks 4–7), and finally retested four weeks after the discontinuation of the shampoo therapy (week 11). The authors reported no difference in bacterial microbiome diversity over time in either group. On the contrary, a decrease diversity in fungal microbiome (particularly organisms of the genus *Epicoccum* and *Blumeria*) on healthy and atopic skin was seen after the shampoo therapy (week 7) to then increase at the end of the study (week 11).

The second study[29] assessed the effects of a phototherapy protocol, implementing the use of a UVB-light skin therapy system (308 nm excimer light) applied weekly for two months, on the cutaneous microbiome of atopic ($n=10$) dogs. In this study, dogs were allowed to be on other treatments for AD (e.g. lokivetmab, oclacitinib, topical antimicrobials) if initiated at least three months before the study. At the end of the study, phototherapy was associated with a significantly increased relative abundance of Actinobacteria and Cyanobacteria in atopic dogs. In addition, phototherapy resulted in an overall decrease in *S. pseudintermedius* in atopic dogs.

## SUMMARY OF CUTANEOUS MICROBIOME

In summary, in the past 10 years, the amount of literature on the cutaneous and aural microbiome in canine AD has significantly increased. Many studies have reported a significant dysbiosis on the skin and in the external ear canals of atopic dogs with a predominance of staphylococcal organisms compared to healthy dogs. However, as mentioned before, if the dysbiosis is a cause or a consequence of the AD status is undetermined at this time. Additionally, researchers have started to look into the effects of topical therapy

(shampoo versus phototherapy) on cutaneous microbiome. These studies include a very small number of dogs and the results should be interpreted cautiously. They are an indication that larger studies are needed to assess the effect of the topical antimicrobial therapy on the microbiome of atopic dogs.

## UPDATE ON HOST DEFENCE PEPTIDES

Along with the structural changes of the cutaneous barrier described above, alterations of the chemical and immunological barriers also have been investigated in atopic dogs. In particular, the role that host defence peptides (HDPs; also known as antimicrobial peptides) play in AD has been extensively studied in humans and to some extent in dogs as well. Several studies identified altered amounts of HDPs in lesional and nonlesional canine atopic skin.[43–45] However, studies are needed to assess if these alterations are due to a compromised mechanism of production and secretion[46,47] or because of structural changes of HDPs in atopic dogs.

HDPs represent one of the most important lines of defence against microbial invasion. Along with their powerful antimicrobial action, HDPs also are potent immunomodulatory molecules acting as a bridge between innate and adaptive immunity. Several HDPs have been identified in the skin of healthy and atopic dogs.[1,48] As in humans, alterations to the expression and/or structure of HDPs have been hypothesised to increase susceptibility to skin infection in dogs with AD.[1] Over the years, few studies on the expression of HDPs in atopic skin have been published. Such studies have shown increased gene expression of HDPs, mainly of β-defensins and cathelicidin, in the skin of atopic dogs when compared to healthy skin,[45] particularly with active infection.[44] Interestingly, the increased gene expression (mRNA) was not always accompanied by a similar increase at the protein level.[44,45] These results suggested potential dysregulation in the synthesis of HDPs in atopic skin.

Two recent studies[46,47] have demonstrated qualitative and quantitative alterations of the secretion of HDPs in the skin of atopic dogs. In particular, one study comparing the skin-surface wash fluid from healthy and atopic dogs showed that, despite a similar amount of HDPs, skin wash fluid from atopic dogs had significantly lower inhibitory activity against *S. pseudintermedius*. This suggests that HDPs in atopic dogs exhibit poorer antimicrobial activity.[46] More recently, another study analysed HDP expression in skin explants harvested from healthy and atopic dogs via indirect immunofluorescence (intracellular accumulation), enzyme-linked immunosorbent assay (secretion) and immuno-scanning electron microscopy (iSEM; surface expression).[47] Atopic skin had higher levels of HDPs retained inside the keratinocytes and a lower level secreted in the supernatant compared to healthy skin.[47] Using iSEM, it was evident that canine β-defensin 103 was retained on the outermost layer of the SC and the number of bacteria-adhered peptides was higher in atopic when compared to healthy skin.[47]

As reported above, until recently the amount and function of HDPs has only been investigated in the skin of healthy and atopic dogs. In 2023, Santoro[49] published the first report on the amount and antimicrobial activity of aural HDPs in healthy and atopic dogs. In this report, the author described a decreased amount of cBD3-like and cCath in noninfected ears of atopic dogs when compared with healthy ears. Measurable antimicrobial activity was very variable and considered minimal by the author.

In summary, these studies suggest that atopic skin shows higher HDP gene expression nonassociated with an increase in protein expression. Additionally, there is dysregulation in the secretion (tendency to be retained in the keratinocytes), dispersion (tendency to remain attached on the skin surface), and probably antimicrobial efficacy (lower antibacterial inhibitory effect) of atopic compared to healthy HDPs. Thus, the involvement of HDPs in the pathogenesis of skin infections in dogs with AD may not be related to their levels, and rather to their functionality and secretion.

## CONCLUSIONS

In conclusion, in the past seven years, a moderate amount of research has been published on the effect of skin barrier integrity in the pathogenesis of canine AD. Such research has been focused not only on structural and immunological changes in the skin barrier, but also on the alterations occurring in the cutaneous and aural microbiome of atopic dogs. The results of these studies confirm the extremely complex nature of canine AD. Although the nonhomogeneous results among studies makes their interpretation difficult, it also favours the concept of AD being a syndrome with more than a single entity. In particular, it is evident that there are several subsets of this disease and intrinsic alterations of skin barrier may play a significant role in some dogs, while the imbalance of the immune system may play a larger role in others. Such recognition is essential to design an appropriate treatment plan. In fact, dogs with intrinsic alterations of skin barrier may benefit more from topical therapies aimed to restore it. However, dogs with a predominant imbalance of the immune response may benefit more from anti-inflammatory medications.

Also, newer studies have investigated the role that cutaneous and aural microbiota play in the development and/or worsening of canine AD. Unfortunately, such studies are mainly descriptive and still not able to elucidate the pathogenetic role of dysbiosis in canine AD. Nevertheless, this information is essential to move forward understanding the pathogenesis of this complex disease and to better guide the development of new therapeutic options.

### AUTHOR CONTRIBUTIONS

**Domenico Santoro:** Conceptualization; investigation; writing – original draft; writing – review and editing. **Manolis Saridomichelakis:** Writing – review and editing; conceptualization. **Melissa Eisenschenk:** Conceptualization; writing – review and editing;

project administration. **Chie Tamamoto-Mochizuki:** Writing – review and editing. **Patrick Hensel:** Conceptualization; writing – review and editing. **Cherie Pucheu-Haston:** Conceptualization; writing – review and editing.

## ACKNOWLEDGEMENTS

This article was reviewed by members of the International Committee on Allergic Diseases in Animals (Frane Banovic, Emmanuel Bensignor, Douglas DeBoer, Graig Griffin, Ralf Mueller, Tim Nuttall and Christine Prost) whose contributions to this work are gratefully acknowledged.

## FUNDING INFORMATION

This study was self-funded.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest relevant to this article.

## ORCID

*Domenico Santoro* https://orcid.org/0000-0002-4893-4289
*Manolis Saridomichelakis* https://orcid.org/0000-0001-8308-3371
*Melissa Eisenschenk* https://orcid.org/0000-0002-4764-4730
*Chie Tamamoto-Mochizuki* https://orcid.org/0000-0001-6423-7718
*Patrick Hensel* https://orcid.org/0000-0002-3845-7992
*Cherie Pucheu-Haston* https://orcid.org/0000-0003-1916-7188

## REFERENCES

1. Santoro D, Marsella R, Pucheu-Haston CM, Eisenschenk MNC, Nuttall T, Bizikova P. Review: pathogenesis of canine atopic dermatitis: skin barrier and host–micro-organism interaction. Vet Dermatol. 2015;26:84-e25.
2. Cobiella D, Archer L, Bohannon M, Santoro D. Pilot study using five methods to evaluate skin barrier function in healthy dogs and in dogs with atopic dermatitis. Vet Dermatol. 2019;30:121-e34.
3. Bradley CW, Morris DO, Rankin SC, Cain CL, Misic AM, Houser T, et al. Longitudinal evaluation of the skin microbiome and association with microenvironment and treatment in canine atopic dermatitis. J Invest Dermatol. 2016;136:1182–90.
4. Bashir SJ, Chew AL, Anigbogu A, Dreher F, Maibach HI. Physical and physiological effects of stratum corneum tape stripping. Skin Res Technol. 2001;7:40–8.
5. Yoon J-S, Nishifuji K, Sasaki A, Ide K, Ishikawa J, Yoshihara T, et al. Alteration of stratum corneum ceramide profiles in spontaneous canine model of atopic dermatitis. Exp Dermatol. 2011;20:732–6.
6. Stahl J, Paps J, Bäumer W, Olivry T. *Dermatophagoides farinae* house dust mite allergen challenges reduce stratum corneum ceramides in an experimental dog model of acute atopic dermatitis. Vet Dermatol. 2012;23:497-e97.
7. Reiter LV, Torres SM, Wetz PW. Characterization and quantification of ceramides in the nonlesional skin of canine patients with atopic dermatitis compared with controls. Vet Dermatol. 2009;20:260–6.
8. Shimada K, Yoon J-S, Yoshihara T, Iwasaki T, Nishifuji K. Increased transepidermal water loss and decreased ceramide content in lesional and non-lesional skin of dogs with atopic dermatitis. Vet Dermatol. 2009;20:541–6.
9. Chermprapai S, Broere F, Gooris G, Schlotter YM, Rutten VPMG, Bouwstra JA. Altered lipid properties of the stratum corneum in canine atopic dermatitis. Biochim Biophys Acta Biomembr. 2018;1860:526–33.
10. Drislane C, Irvine AD. The role of filaggrin in atopic dermatitis and allergic disease. Ann Allergy Asthma Immunol. 2020;124:36–43.
11. Chervet L, Galichet A, McLean WHI, Chen H, Suter MM, Roosje PJ, et al. Missing C-terminal filaggrin expression, NFkappaB activation and hyperproliferation identify the dog as a putative model to study epidermal dysfunction in atopic dermatitis. Exp Dermatol. 2010;19:e343–6.
12. Wood SH, Ollier WE, Nuttall T, McEwan NA, Carter SD. Despite identifying some shared gene associations with human atopic dermatitis the use of multiple dog breeds from various locations limits detection of gene associations in canine atopic dermatitis. Vet Immunol Immunopathol. 2010;138:193–7.
13. Hensel P, Santoro D, Favrot C, Hill P, Griffin C. Canine atopic dermatitis: detailed guidelines for diagnosis and allergen identification. BMC Vet Res. 2015;11:196.
14. Wu Z, Hansmann B, Meyer-Hoffert U, Gläser R, Schröder J-M. Molecular identification and expression analysis of filaggrin-2, a member of the S100 fused-type protein family. PloS One. 2009;4:e5227.
15. Alberola G, Schroder J-M, Froment C, Simon M. The amino-terminal part of human FLG2 is a component of cornified envelopes. J Invest Dermatol. 2019;139:1395–7.
16. Combarros D, Cadiergues M-C, Simon M. Update on canine filaggrin: a review. Vet Q. 2020;40:162–8.
17. Santoro D, Marsella R, Ahrens K, Graves TK, Bunick D. Altered mRNA and protein expression of filaggrin in the skin of a canine animal model for atopic dermatitis. Vet Dermatol. 2013;24:329–36, e73.
18. Marsella R, Santoro D, Ahrens K, Thomas AL. Investigation of the effect of probiotic exposure on filaggrin expression in an experimental model of canine atopic dermatitis. Vet Dermatol. 2013;24:260-e57.
19. Marsella R, Papastavros V, Ahrens K, Santoro D. Decreased expression of caspase-14 in an experimental model of canine atopic dermatitis. Vet J. 2016;209:201–3.
20. Fanton N, Santoro D, Cornegliani L, Marsella R. Increased filaggrin-metabolizing enzyme activity in atopic skin: a pilot study using a canine model of atopic dermatitis. Vet Dermatol. 2017;28:479-e111.
21. Olivry T, Paps JS, Amalric N. Transient and reversible reduction of stratum corneum filaggrin degradation products after allergen challenge in experimentally mite-sensitised atopic dogs. Vet Dermatol. 2022;33:62-e20.
22. Olivry T, Dunston SM. Expression patterns of superficial epidermal adhesion molecules in an experimental dog model of acute atopic dermatitis skin lesions. Vet Dermatol. 2015;26:53–6, -e17-8.
23. Kim H-J, Cronin M, Ahrens K, Papastavros V, Santoro D, Marsella R. A comparative study of epidermal tight junction proteins in a dog model of atopic dermatitis. Vet Dermatol. 2016;27:40-e11.
24. Roussel AJJ, Bruet V, Marsella R, Knol AC, Bourdeau PJ. Tight junction proteins in the canine epidermis: a pilot study on their distribution in normal and in high IgE-producing canines. Can J Vet Res. 2015;79:46–51.
25. Marsella R, Ahrens K, Wilkes R. Differences in behavior between normal and atopic keratinocytes in culture: pilot studies. Vet Sci. 2022;9:329.
26. Kobielak A, Boddupally K. Junctions and inflammation in the skin. Cell Commun Adhes. 2014;21:141–7.
27. Rodrigues Hoffmann A, Patterson AP, Diesel A, Lawhon SD, Ly HJ, Elkins Stephenson C, et al. The skin microbiome in healthy and allergic dogs. PloS One. 2014;9:e83197.
28. Chermprapai S, Ederveen THA, Broere F, Broens EM, Schlotter YM, van Schalkwijk S, et al. The bacterial and fungal microbiome of the skin of healthy dogs and dogs with atopic dermatitis and the impact of topical antimicrobial therapy, an exploratory study. Vet Microbiol. 2019;229:90–9.

29. Park J-Y, Kim S-M, Kim J-H. Efficacy of phototherapy with 308-nm excimer light for skin microbiome dysbiosis and skin barrier dysfunction in canine atopic dermatitis. Front Vet Sci. 2021;8:762961.
30. Uchiyama J, Osumi T, Mizukami K, Fukuyama T, Shima A, Unno A, et al. Characterization of the oral and faecal microbiota associated with atopic dermatitis in dogs selected from a purebred Shiba Inu colony. Lett Appl Microbiol. 2022;75:1607–16.
31. Rodriguez-Campos S, Rostaher A, Zwickl L, Fischer N, Brodard I, Vidal S, et al. Impact of the early-life skin microbiota on the development of canine atopic dermatitis in a high-risk breed birth cohort. Sci Rep. 2020;10:1044.
32. Kim S-W, Kim J-H. Establishing an experimental model for canine atopic dermatitis through epicutaneous application of *Dermatophagoides farinae*. Front Vet Sci. 2022;9:1015915.
33. Rostaher A, Morsy Y, Favrot C, Unterer S, Schnyder M, Scharl M, et al. Comparison of the gut microbiome between atopic and healthy dogs – preliminary data. Animals (Basel). 2022;12:2377.
34. Tang S, Prem A, Tjokrosurjo J, Sary M, Van Bel MA, Rodrigues-Hoffmann A, et al. The canine skin and ear microbiome: a comprehensive survey of pathogens implicated in canine skin and ear infections using a novel next-generation-sequencing-based assay. Vet Microbiol. 2020;247:108764.
35. Weese JS. The canine and feline skin microbiome in health and disease. Vet Dermatol. 2013;24:137–45, e131.
36. Rodrigues HA. The cutaneous ecosystem: the roles of the skin microbiome in health and its association with inflammatory skin conditions in humans and animals. Vet Dermatol. 2017;28:60-e15.
37. Older CE, Rodrigues Hoffmann A, Hoover K, Banovic F. Characterization of cutaneous bacterial microbiota from superficial pyoderma forms in atopic dogs. Pathogens. 2020;9:638.
38. Meason-Smith C, Diesel A, Patterson AP, Older CE, Mansell JM, Suchodolski JS, et al. What is living on your dog's skin? Characterization of the canine cutaneous mycobiota and fungal dysbiosis in canine allergic dermatitis. FEMS Microbiol Ecol. 2015;91:fiv139.
39. Meason-Smith C, Olivry T, Lawhon SD, Hoffmann AR. *Malassezia* species dysbiosis in natural and allergen-induced atopic dermatitis in dogs. Med Mycol. 2020;58:756–65.
40. Pierezan F, Olivry T, Paps JS, Lawhon SD, Wu J, Steiner JM, et al. The skin microbiome in allergen-induced atopic dermatitis. Vet Dermatol. 2016;27:332-e82.
41. Ngo J, Taminiau B, Fall PA, Daube G, Fontaine J. Ear canal microbiota – a comparison between healthy dogs and atopic dogs without clinical signs of otitis externa. Vet Dermatol. 2018;29:425-e140.
42. Apostolopoulos N, Glaeser SP, Bagwe R, Janssen S, Mayer U, Ewers C, et al. Description and comparison of the skin and ear canal microbiota of non-allergic and allergic German shepherd dogs using next generation sequencing. PloS One. 2021;16:e0250695.
43. Lancto CA, Torres SMF, Hendrickson JA, Martins KV, Rutherford MS. Altered expression of antimicrobial peptide genes in the skin of dogs with atopic dermatitis and other inflammatory skin conditions. Vet Dermatol. 2013;24:414–21, e90.
44. Santoro D, Bunick D, Graves TK, Segre M. Evaluation of canine antimicrobial peptides in infected and noninfected chronic atopic skin. Vet Dermatol. 2013;24:39–47, e10.
45. Santoro D, Marsella R, Bunick D, Graves TK, Campbell KL. Expression and distribution of canine antimicrobial peptides in the skin of healthy and atopic beagles. Vet Immunol Immunopathol. 2011;144:382–8.
46. Santoro D. Evaluation of the secretion of antimicrobial peptides and antimicrobial effect of skin wash in atopic and healthy dogs: a preliminary study. Vet Dermatol. 2018;29:402-e132.
47. Santoro D, Archer L, Kelley K. A defective release of host defense peptides is present in canine atopic skin. Comp Immunol Microbiol Infect Dis. 2019;65:65–9.
48. Leonard BC, Affolter VK, Bevins CL. Antimicrobial peptides: agents of border protection for companion animals. Vet Dermatol. 2012;23:177-e36.
49. Santoro D. Comparison of the quantity and antimicrobial activity of host defence peptides in ear canals between healthy and atopic dogs: a preliminary study. Vet Dermatol. 2023;34:452–9.

**How to cite this article:** Santoro D, Saridomichelakis M, Eisenschenk M, Tamamoto-Mochizuki C, Hensel P, Pucheu-Haston C. Update on the skin barrier, cutaneous microbiome and host defence peptides in canine atopic dermatitis. Vet Dermatol. 2023;00:1–10. https://doi.org/10.1111/vde.13215

**Résumé**

**Contexte:** La dermatite atopique (DA) canine est une maladie inflammatoire cutanée complexe associée à des altérations du microbiome cutané, de l'immunité et de la barrière cutanés. Cette revue fait le point concernant les données actuelles sur les défauts de la barrière cutanée et sur le dysfonctionnement du microbiome cutané dans la DA canine.

**Objectif:** À cet effet, les bases de données bibliographiques, les résumés et les proceedings des réunions internationales sur la barrière et le microbiome cutanés publiés entre 2015 et 2023 sont examinés.

**Résultats:** Depuis la dernière mise à jour concernant la pathogénie de la DA canine, publiée par le Comité international sur les affections allergiques des animaux en 2015 (ICADA), 49 articles ont été publiés sur la fonction de barrière cutanée, l'immunité innée et le microbiome cutanés/auriculaires chez les chiens atopiques. Le dysfonctionnement de la barrière et la dysbiose microbienne cutanés sont des acteurs essentiels dans la pathogénie de la DA canine. On ne sait toujours pas si ces altérations sont primaires ou secondaires à l'inflammation cutanée, bien que certaines données soutiennent leur implication primaire dans l'étiopathogénie de la DA canine.

**Conclusion et pertinence clinique:** Bien que de nombreuses études aient été publiées depuis 2015, la compréhension de l'interaction cutanée entre l'hôte et les microbes n'est toujours pas claire, tout comme l'implication de la dysbiose cutanée dans le développement et/ou l'aggravation de la DA canine. D'autres études sont nécessaires pour concevoir de nouvelles approches thérapeutiques visant à restaurer la barrière cutanée, à augmenter et à optimiser les défenses naturelles cutanées.

**Resumen**

**Introducción:** la dermatitis atópica (cAD) canina es una enfermedad inflamatoria compleja de la piel asociada con alteraciones del microbioma cutáneo, inmunológicas y de la barrera cutánea. Esta revisión resume la evidencia actual acerca de los defectos de la barrera cutánea y la disfunción del microbioma cutáneo en la AD canina.

**Objetivo:** Para ello, se revisaron bases de datos de citas en línea, resúmenes y actas de reuniones internacionales sobre barrera cutánea y microbioma cutáneo publicados entre 2015 y 2023.

**Resultados:** Desde la última actualización sobre la patogénesis de la AD canina, publicada por el Comité Internacional de Enfermedades Alérgicas de los Animales en 2015, se han publicado 49 artículos sobre la función de la barrera cutánea, la inmunidad innata cutánea/aural y el microbioma cutáneo/aural en perros atópicos. La disfunción de la barrera cutánea y la disbiosis microbiana cutánea son factores esenciales en la patogénesis de la AD canina. Aún no está claro si dichas alteraciones son primarias o secundarias a la inflamación cutánea, aunque alguna evidencia respalda su participación primaria en la patogénesis de la AD canina.

**Conclusión y relevancia clínica:** Aunque se han publicado muchos estudios desde 2015, la comprensión de la interacción huésped-microbio a nivel cutáneo aún no está clara, al igual que el papel que desempeña la disbiosis cutánea en el desarrollo y/o empeoramiento de la AD canina. Se necesitan más estudios con el objetivo de diseñar nuevos enfoques terapéuticos para restaurar la barrera cutánea, aumentar y optimizar las defensas naturales cutáneas y reequilibrar el microbioma cutáneo.

**要約**

**背景:** 犬アトピー性皮膚炎(AD)は、皮膚マイクロバイオーム、免疫学的変化、皮膚バリア変化を伴う複雑な炎症性皮膚疾患である。本総説では、犬のADにおける皮膚バリア欠損および皮膚マイクロバイオームの機能不全に関する現在のエビデンスを要約した。

**目的:** この目的のために、2015年から2023年の間に発表された皮膚バリアおよび皮膚マイクロバイオームに関する国際会議オンライン引用データベース、抄録、プロシーディングをレビューした。

**結果:** 2015年に動物のアレルギー性疾患に関する国際委員会(International Committee on Allergic Diseases of Animals)によって発表された犬ADの病態に関する最後のアップデート以降、アトピー犬の皮膚バリア機能、皮膚/耳における自然免疫、皮膚/耳におけるマイクロバイオームに関する49の論文が発表された。皮膚バリア機能障害および皮膚微生物ディスバイオシスは、犬のADの発症に不可欠な因子である。このような変化が皮膚炎症の一次的なものなのか二次的なものなのかはまだ不明であるが、犬ADの病因に一次的に関与していることを支持するエビデンスもあった。

**結論と臨床的関連性:** 2015年以降、多くの研究が発表されているが、皮膚における宿主と微生物の相互作用に関する理解はまだ不明であり、また、犬のADの発症および/または悪化において皮膚微生物ディスバイオシスが果たす役割も不明である。皮膚のバリア機能を回復させ、皮膚の自然防御機能を高め、最適化し、皮膚マイクロバイオームのバランスを整えるための新たな治療アプローチをデザインすることを目的とした、さらなる研究が必要である。

**摘要**

**背景:** 犬特应性皮炎(AD)是一种复杂的炎症性皮肤病,与皮肤微生物组、免疫和皮肤屏障的改变有关。这篇综述总结了目前关于犬AD皮肤屏障缺陷和皮肤微生物组功能障碍的证据。

**目的:** 为此,回顾了2015年至2023年间发表的皮肤屏障和皮肤微生物组国际会议的在线引文数据库、摘要和会议记录。

**结果:** 自2015年国际动物过敏性疾病委员会发表关于犬AD发病机制的最后一次更新以来,已经发表了49篇关于特应性犬的皮肤屏障功能、皮肤/耳道先天免疫和皮肤/耳道微生物组的文章。皮肤屏障功能障碍和皮肤微生物微生态失调是犬AD发病机制中的重要因素。目前尚不清楚这种改变是皮肤炎症的原发性还是继发性原因,尽管一些证据支持它们主要参与犬AD的发病机制。

**结论和临床相关性:** 尽管自2015年以来已经发表了许多研究,但对皮肤宿主-微生物相互作用的理解仍然不清楚,皮肤微生态失调在犬AD的发展和/或恶化中所起的作用也不清楚。还需要更多的研究来设计新的治疗方法来恢复皮肤屏障,以增加和优化皮肤的自然防御,并重新平衡皮肤微生物组。

**Resumo**

**Contexto:** A dermatite atópica (DA) é uma dermatopatia inflamatória complexa associada a alterações imunológicas, de barreira cutânea e no microbioma cutâneo. Esta revisão resume as evidências atuais acerca dos defeitos de barreira cutânea e disfunções do microbioma cutâneo na DA canina.

**Objetivo:** Para isso, foram revisados anais e resumos de congressos internacionais e citações em bases de dados online sobre barreira cutânea e microbioma cutâneo entre 2015 e 2023.

**Resultados:** Desde a última atualização na patogênese da DA canina, publicada pelo *International Committee on Allergic Diseases of Animals em* 2015, 49 artigos foram publicados sobre função da barreia cutânea, imunidade inata cutânea/aural e microbioma cutâneo/aural em cães atópicos. Disfunção de barreira cutânea e disbiose cutânea microbiana são fatores essenciais na patogênese da DA canina. Ainda não se sabe exatamente se estas alterações são primárias ou secundárias à inflamação cutânea, apesar de algumas evidências corroborarem com o seu envolvimento primário na DA canina.

**Conclusões e Relevância Clínica:** Apesar de muitos estudos terem sido publicados desde 2015, a compreensão da interação microbioma-hospedeiro permanece não esclarecida, bem como o papel da disbiose cutânea no desenvolvimento e/ou agravamento da DA canina. Mais estudos são necessários para o desenvolvimento de novas abordagens terapêuticas para restaurar a barreira cutânea, para intensificar e otimizar as defesas naturais da pele e reequilibrar o microbioma cutâneo.

**Zusammenfassung**

**Hintergrund:** Die atopische Dermatitis des Hundes (AD) ist eine komplexe entzündliche Erkrankung, die mit Veränderungen im kutanen Mikrobiom, der immunologischen Barriere und der Hautbarriere einhergeht. Diese Review fasst die momentane Evidenz über die Defekte der Hautbarriere und der Dysfunktion des kutanen Mikrobioms bei der AD des Hundes zusammen.

**Ziele:** Für diese Studie wurden Online-Datenbanken, Abstacts und Proceedings von internationalen Treffen auf Publikationen über die Hautbarriere und das kutane Mikrobiom in der Zeit zwischen 2015 und 2023 durchgesehen.

**Ergebnisse:** Seit dem letzten Up-date über die Pathogenese der AD des Hundes, das vom International Committee über allergische Erkrankungen bei Tieren 2015 publiziert wurde, sind 49 Artikel über die Funktion der Hautbarriere, über die angeborene Immunität der Haut/der Ohren und das kutane/aurale Mikrobiom bei atopischen Hunden publiziert worden. Die Dysfunktion der Hautbarriere und die kutane mikrobielle Dysbiose sind essenzielle Spieler bei der Pathogenese der AD des Hundes. Es ist noch immer unklar, ob derartige Veränderungen primär oder sekundär mit der kutanen Entzündung auftreten, obwohl es einige Evidenz zur Unterstützung der primären Beteiligung an der Pathogenese der AD des Hundes gibt.

**Schlussfolgerungen und klinische Bedeutung:** Obwohl seit 2015 viele Studien publiziert worden sind, ist das Verständnis über die kutane Interaktion zwischen Wirt und Mikroben noch immer unklar. Das gleich gilt für die Rolle, die die kutane Dysbiose bei der Entwicklung und/oder Verschlechterung der AD des Hundes spielt. Es sind weitere Studien nötig, die darauf abzielen sollten ein neues Design zu erstellen für therapeutischen Herangehensweisen zur Wiederherstellung der Hautbarriere, zur Verstärkung oder Optimierung der Naturabwehr der Haut und für das Finden einer neuen Balance des kutanen Mikrobioms.