Skin barrier function

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The importance of skin barrier function for various skin disorders has been increasingly recognised over the last 10 years in human and veterinary medicine. Barrier dysfunction is a typical feature of human atopic dermatitis (AD) and allergic diseases, allowing for the penetration of allergens, microorganisms and other irritants into the skin and eliciting inflammation, bacterial colonization and allergen sensitization. The epidermis functions as the primary defence layer to the external environment, and includes epidermal cells and a cornified layer, but most of the barrier function is regulated by the stratum corneum (SC) and the tight junction which resides at the level of the stratum granulosum. When the SC is compromised, usually due to decreased levels of SC lipids, mechanical trauma resulting from extensive scratching that is precipitated by an intensive itching sensation is observed.

SC lipids in skin barrier function

In humans, several studies have suggested that reduced levels of ceramides, the major constituents of intercellular lipids in the stratum corneum are involved in defective barrier function of AD. Lower levels of ceramides in the SC are thought to accelerate trans-epidermal water loss (TEWL) and decrease water capacitance resulting in atopic dry skin. Additionally, impairment of the barrier function of the SC may facilitate percutaneous entry of aeroallergens that might provoke an immune reaction. Thus, the loss of barrier function in the SC might be one of the key roles in the development and aggravation of AD in humans.

In dogs, electron microscopic analysis revealed that the continuity and the thickness of the intercellular lipid lamellae are significantly reduced in non-lesional atopic skin when compared with normal canines. Alternatively, Chesney reported that the skin hydration and water dynamics of the skin of atopic dogs did not differ from those of normal dogs. Currently, the association of altered lipid barrier function in the pathophysiology of canine AD is not fully understood. Recently, a new method of measuring TEWL on canine skin with a closed chamber device showed less variable measurements than the conventional open-chamber method. Furthermore, it was reported that TEWL was increased in canine skin by disruption of the barrier function via tape stripping. Thus, TEWL measured by a closed chamber device is thought to reflect the skin barrier function in dogs as well as in humans. TEWL, in both lesional and non-lesional skin of dogs with atopic dermatitis, exhibited significantly high values compared with non-atopic dog skin. This result may indicate that canine atopic dermatitis is possibly to relate to decreased skin barrier function.

Ceramides make up approximately 30% of skin lipids and rest of skin lipids are cholesterols(60%) and free fatty acids (10%) in normal dog skin. Ceramides are composites of sphingosine and fatty acids, and are capable of holding a large amount of water through the OH- terminal. Therefore, a defect in ceramides of the SC may elicit skin dryness thereby leading to sensitive skin. In a previous study, a topical lipid preparation containing ceramides, free fatty acids and cholesterol was applied to five dogs with atopic dermatitis and after repeated application of the lipid preparation, the lamellar layer of the SC was observed to have increased. The decreased proportion of ceramide in lesional and non-lesional skin of dogs with atopy has been reported. This study demonstrated a decreased ratio of ceramide to free-fatty acids and cholesterol. There were negative correlations between relative ceramide amounts and TEWL suggesting decreased ceramides may elicit dryness of skin and skin barrier dysfunction. Reiter et al. demonstrated that decreased levels of specific ceramide subclasses 1 and 9 might be involved in impaired barrier function in canine atopic dermatitis.

Filaggrin mutations in human and canine atopic dermatitis

Atopic dermatitis in humans and dogs has been regarded as a genetic disorder with a familial occurrence or breed predilection. It is believed that skin barrier dysfunction is an essential feature of atopic dermatitis and allergic diseases in general. In human atopic dermatitis, it is reported that 12.5–48% of patients have mutations in filaggrin. Thus, a loss-of-function filaggrin mutation is thought to be a risk factor for atopic dermatitis in humans. Marsella et al. compared immunohistochemical staining of filaggrin between normal and house dust mite sensitized beagles and found no obvious correlation between immunostaining and clinical scores. Recently,
a linkage analysis was investigated in non-atopic and atopic West Highland White Terriers (WHWT) and in this study, a large causative role of the FLG orthologue in atopy was excluded. There are no studies demonstrating an obvious relationship between FLG mutations and risk of atopic dermatitis in dogs, but future studies should hopefully elucidate the degree to which skin barrier function contributes to the pathogenesis of canine atopic dermatitis.

References
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