Interleukin 8 and Host Defense Peptides contribute to the Innate Immune Response against Digital Dermatitis and supplement the 5 M-stages scoring system in dairy cattle

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Bovine digital dermatitis (DD) is an infectious disease in the foot of cows, mostly caused by *Treponema* spp, which is characterized by ulcerative and necrotic lesions with no effective treatment. Affected cattle develop lameness that is reflected in reduced milk production and lower reproductive rates, premature culling and weight loss. While DD is usually diagnosed by the 5 M-stages scoring system in the diseased foot, the inflammatory reaction and the immune role in the bovine skin have not been adequately addressed. In this study, the bovine skin innate response was investigated in cows afflicted with clinical lameness due to DD and correlated with presence of *Treponema spp.* and M- stages scoring. Our results show that cattle suffering from acute DD (M1/M2) had significant neutrophil infiltration in the epidermis and increased transcription gene expression of β-defensin tracheal antimicrobial peptides (TAP), when compared to control skin tissue. These acute stages also corresponded to elevated local IL-8 transcription gene expression. Conversely, anti-inflammatory IL-10 and cathelicidins, bovine myeloid antimicrobial peptide 28 (BMAP-28), were elevated in healthy cows or in those cows at later stages of DD (M4) compared to acute DD stages. These findings indicate that the neutrophil influx, contributed by IL-8 and β-defensin are key markers in acute DD stages and essential for bacterial clearance. Cathelicidins and IL-10 seem crucial in the healing or recovery status of the disease. This work has unveiled fundamental steps in the pathogenesis of DD and revealed biomarkers(cytokines and host defense peptides) and novel therapeutic targets to the dairy industry that complement the traditional M scoring system.