Contribution of Naturally Produced Host Defenses to Inflammation and Resolution of Digital Dermatitis in Dairy Cattle

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Background: Digital Dermatitis (DD) is a common infectious disease in dairy cattle, caused by *Treponema* spp., provoking painful lesions around the hoof. Cows afflicted with DD suffer experience discomfort and lameness and concomitant reduced milk production and premature culling. This drastically impacts both the animal welfare and sustainability of the dairy industry. Naturally produced defense mechanisms remain unexplored in cattle even though they are key to understanding the pathogenesis of skin diseases, such as DD. In this regard, cows abundantly secrete host defense peptides (HDPs), such as cathelicidins, by skin epithelial cells and surrounding neutrophils. Interestingly, mice deficient in cathelicidins exhibit exacerbated dermatitis and increased pathogen burden when challenged by infectious agents. However, the importance of HDPs (cathelicidins) for skin defenses in cattle and their role in DD remains unknown. **Objective:** We aimed to determine how naturally occurring HDPs (cathelicidins) aid in the control of DD caused by *Treponema* spp.

Materials and Methods: Skin epithelial cells (HaCaT keratinocytes) were exposed to *Treponema* spp. for 6 and 24 h. Cytokines associated with inflammation (Il-10, IL-8 TNF-alpha, IFN-gamma and TLR-4) were measured for gene expression (rtPCR). Skin biopsies obtained from dairy cattle suffering with DD (stages M0 to M4.1) were collected and RNA extracted to measure the expression of bovine HDPs (Tracheal Antimicrobial Peptide, TAP and; Lingual Antimicrobial Peptide, LAP). **Results:** HaCaT keratinocytes exposed to *Treponema* spp. showed increased gene expression of cathelicidins and TLR-4. Cattle with acute DD lesions expressed varying levels of TAP and LAP at the individual level. However cows with DD M4.1 stage had the highest level of HDP expression when compared to cattle with M0 stage skin.

Implications: Exposure to *Treponema* spp. induced increases in HDP production by skin epithelial cells. Cows afflicted with DD also responded producing naturally occurring HDPs to infection. High expression of HDPs is correlated with chronic stages of DD. This project is advancing the roles and mechanisms of HDPs (cathelicidins) in pathogen clearance and resolution of DD in cows. Further investigations will provide insight into the use of these HDP as antimicrobial and immunomodulatory therapeutics in production animals. This information is greatly beneficial for the dairy industry since the treatment of DD with conventional antibiotics or untested chemicals is becoming unsustainable due to the emergence of antimicrobial resistance and residues in milk.