

Developing Novel Therapeutic Alternatives for Bovine Digital Dermatitis

Priyoshi Lahiri, Makaela Douglas, Karin Orsel, Herman W. Barkema and Eduardo R. Cobo

Dept. of Production Animal Health, Faculty of Veterinary Medicine, University of Calgary, Calgary, Alberta, Canada Email: priyoshi.lahiri@ucalgary.ca

Digital dermatitis (DD) is an ulcerative and painful skin disease of the foot in cattle, mostly associated with *Treponemes* bacteria, where skin healing is severely impaired in DD and oxytetracycline is the most effective treatment to date. DD is common in dairy cattle (affecting up to 15% of cows and 94% of herds in Alberta), resulting in economic and major welfare concerns. Using oxytetracycline in treating DD increases the burden of antimicrobial resistance in dairy cattle in Alberta, leading to antibiotic residuals in the food chain. Therefore, developing a novel therapeutic for DD is indispensable to produce healthy dairy products. Our research has established that cows with active DD lesions display accumulation of neutrophils. Timely removal of neutrophils by distinct phenotypes of macrophages is necessary for the skin wound healing process to begin. Neutrophils contain matrix metalloproteinases (MMPs) that regulate tissue remodeling during skin inflammation. Increased neutrophil infiltration and dysregulated protease or MMP activity exacerbate acute and chronic skin wounds in inflammatory skin disorders. Our research objective is to understand why foot skin does not heal in DD and how impaired healing function can be reinstated. Our first aim is to determine the influence of pro-inflammatory and anti-inflammatory macrophages in skin inflammation during active stage (M2) of DD. Our second aim is to perform MMP activity analysis in DD lesions obtained from DD cattle hooves at both acute and chronic stages of DD to find out whether upregulation of MMP activity is associated with tissue destruction in DD. Reducing inflammation and promoting wound healing without the use of antibiotics represent a novel therapeutic approach which aim to heal refractory DD ulcers and chronicity in order to reduce lameness in dairy cattle with less reliance on antibiotics, facilitating welfare and economic benefits for the cattle industry.