Cathelicidin-inducers Butyrate and Vitamin D Modulate the Inflammatory Response in Intestinal Cells Exposed to *Salmonella* spp. Virulent Factors

Chaitanya Shah (cbshah@ucalgary.ca), Ravi Holani (ravi.holani@ucalgary.ca), Qahir Haji (qahir.haji@ucalgary.ca), Eduardo Cobo (ecobo@ucalgary.ca)

Diarrheic enterocolitis caused by oral bacterial infection (e.g. *Salmonella* spp.) affects young dairy cattle with important productive and economically losses in the dairy industry. Moreover, severe cases of infectious enterocolitis lead to septicaemia, dehydration and death. Cathelicidins are small cationic antimicrobial peptides that produced in the intestinal mucosa are essential components of the innate immune defenses. In the search for new therapeutics against neonatal diarrhea in cattle that can control enteric infection and also mitigate harmful intestinal inflammation, we study how to naturally stimulate the production of such cathelicidin peptides in the intestine.

Our model consisted of cultured colonic epithelium (human adenocarcinoma colonic HT-29 cells) exposed to virulent factors of enteric pathogenic *Salmonella enteric Typhimurium* (lipopolysaccharide LPS). We found that natural components such as sodium butyrate and vitamin D (cholecalciferol) stimulated the gene expression of cathelicidins in intestinal cells under these injuring inflammatory conditions. Moreover, concomitant with the production of cathelicidins, butyrate and vitamin D lead to reduced gene expression of pro-inflammatory cytokine tumor necrosis factor alpha (TNF-α) and increased gene expression of anti-inflammatory cytokine interleukin 10 (IL-10).

Our results indicate that cathelicidin inducers such as butyrate and vitamin D may mitigate colitis by reducing the expression of pro-inflammatory factors and/or increasing the expression of anti-inflammatory ones via the action of cathelicidins. Such modulation of the damaging intestinal inflammation and antimicrobial properties of cathelicidins may clinically prevent or cure neonatal diarrheic enterocolitis. This use of non-expensive bio products (butyrate and vitamin D) represents a novel, anti-biotic free way to enhance naturally occurring intestinal defenses while protecting the welfare of calves and the profitability of dairy farmers.

This study is supported by Alberta Livestock Meat Agency Ltd. (ALMA).