Public Abstract

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Title: A series of *in vitro* studies investigating the role of lactoferrin in calf innate immunity.

Neonatal calf mortality rates continue to impact the economic sustainability of the United States cattle industry. Based on data generated from the National Animal Health Monitoring System survey in 2001, 8.9 % of dairy heifer deaths, a translated cost of $800 million dollars, resulted from poor immunity in calves. The majority of diseases which affect cattle are caused by Gram-negative bacteria and clinical signs are attributed to the toxic effects of lipopolysaccharide (LPS), a component of the outer membrane of these pathogens. The central theme of our studies is that bovine colostral lactoferrin (LF) will impact the health of cattle by reducing the effects of lipopolysaccharide (LPS) on the host immune responses. Calves were used as our main experimental model.

Three studies were performed. In the first study, we investigated the ability of lactoferrin to enhance the function of cells involved in bacterial killing. In the second study we examined its ability to interfere with the activation of host cells by LPS. In that study, we also investigated the ability of LF to alter the production of proteins that direct inflammation and in the final study we attempted to determine the mechanism by which it is limiting the production of these proteins. The results from our in vitro studies show that LF limits the ability of LPS to activate host immune cells and in so doing, alters the production of inflammatory proteins by these cells. These findings therefore suggest that the administration of LF to calves succumbing to Gram-negative infections will be useful in reducing the severity of clinical signs and potentially minimizing death. The results of our final study, suggest a novel function of the investigated protein. While further studies are required to confirm this, it appears that lactoferrin is also able to interfere with a subset of intracellular signaling pathways that direct the production of these proteins by immune cells.

Substantiating these results in sick calves will lead to improved productivity within the cattle industry. We also hope that the dependence on conventional antibiotic use will decrease in favor of this novel protein or its peptide derivatives.