**2012F046R Prenatal detection and treatment of calves persistently infected with bovine viral diarrhea virus**

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Background: Bovine viral diarrhea continues to be one of the top two most important indigenous viral diseases in cattle, the other being IBR. In addition to the losses due to BVDV alone, which amount to ~$2 billion annually in North America, BVDV is one of the major components of the bovine respiratory disease (BRD) complex, which affects 14.4% of feedlot placement and causes ~1% mortality. Early diagnosis of cows carrying PI fetuses would allow timely elimination of the PI animals before or immediately after birth to improve BVDV control. However, cows with PI fetuses cannot be accurately and rapidly identified. Recently, we developed a novel approach to analyze cellular responses to a variety of stimuli, known as a kinome analysis. In view of its robust predictive value we planned to use this technology to develop a prenatal detection method for the presence of persistent infection fetuses in pregnant cows.

Objective:

1. Identify the presence of persistently infected (PI) fetuses based on differences in the protein phosphorylation signatures in the blood of pregnant cows
2. Test (phosphor)protein candidates as biomarkers for detection of PI fetuses
3. Evaluate BVDV DNA vaccines for their ability to break tolerance in PI calves

Methods: Pregnant cows were screened and shown to be free of BVDV, BHV-1 and

BRSV. They were challenged with non-cytopathic BVDV or left untreated, and their clinical and immune responses were evaluated.

Outcome: Infection of pregnant cows with ncpBVDV-2 1373 resulted in significant increases of serum interferon gamma (IFN-γ) and alpha (IFN-α). Within the peripheral blood mononuclear cells (PBMCs) of the infected animals, patterns of expression of IFN-γ and IFN-α regulated genes confirmed the ability of these cells to respond to these signals. This finding is supported by temporal kinome analysis that verifies activation of the JAK-STAT signaling pathway, in the PMBCs of the infected animals. Collectively these results demonstrate the induction of a functional Type I immune response in pregnant cows infected with a non-cytopathic strain of BVDV. Importantly, we established for the first time that the kinome arrays may be successfully used to analyze the responses to BVDV infections in cattle in PBMCs, and that blood IFN-γ levels provide a potential biomarker indicative of severe BVDV infection and disease.

Benefits to the industry: An important observation of our research was the fact that kinome analysis can be used to analyze the responses in immune cells from the blood to BVDV (and likely other viral) infections in cattle. Furthermore, based on such analysis we identified a potential biomarker for the severity of BVDV infection, namely IFN-γ levels in the blood, which could be used for early detection of severe BVDV infections, and therefore be of significant benefit to producers.

KTT:

* 1 MSc student and 2 technicians trained
* 1 manuscript submitted to scientific journal
* 1 scientific presentation