Research Summaries I

"Beef and General"

Moderator - Don Hansen, DVM

Genetic -Based Infectious Disease Resistance As A New Health Management Strategy

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Cattle naturally resistant to *Brucella abortus* were bred and progeny from five generations of families were used to study the heritability of genes controlling this trait. Back-crossed calves were phenotyped by challenge with *B. abortus* and the results from genetic analyses indicated that at least two genes control this trait. Macrophages (Mø) from resistant cattle significantly restricted the *in vitro* growth rate of *Mycobacterium bovis, B. abortus* and *Salmonella dublin* which was correlated 83% with *in vivo* resistance. We have cloned the *bovine natural disease resistance associated macrophage protein* (*BovNramp*1) gene and found a significant association between natural resistance and a polymorphism in the 3' untranslated region. hese findings indicate that the polymorphism could be effectively used to genetically select cattle resistant to brucellosis, and potentially salmonellosis, tuberculosis and paratuberculosis. Application of differential display reverse transcriptase PCR (DD RT-PCR) to Mø from resistant or susceptible cattle infected or un-infected with *M. bovis* or *B. abortus* identified several differentially expressed mRNAs two of which were characterized for their potential role in controlling the intracellular growth rate. From infected resistant macrophages, a quantitatively expressed gene with homology to the human calcium dependent potassium channel gene was identified, and a new gene qualitatively expressed was sequenced. Quantitative mRNA expression of *MCP-1, TNFa, TNFaR, GM-CSF, TGFb3, IFNg, IL-1, IL-2, IL-2r, IL-3, IL-4, IL-6, IL-8, L-8r, IL-10, IL-12, Nramp, iNOS* and the two newly identified genes as compared to *GAPD* and *histone* profiled by reverse transcription-T7 RNA dependent amplification (RT-TRDA) from resistant or susceptible challenged and un-challenged Mø revealed unique patterns. Our results suggest that genetic control of macrophage bactericidal mechanisms plays a major role in the control of these zoonotic pathogens and may offer an additional approach to pre-harvest pathogen reduction through genetic selection or genetic engineering.

The Effect of Modified Live Bovine Viral Diarrhea Virus (BVDV) Vaccination During the Third Trimester of Pregnancy in Beef Cows

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Sixteen Brahman-Angus F1 cows (3 years old) were found to be negative for persistent BVDV infection by virus isolation on Buffy coat samples between approximately 180-270 days of gestation. Two weeks later cows

were randomly assigned to vaccinate and nonvaccinate groups. The vaccinate group received a modified live BVDV vaccine (Respancine ® BVD). Post vaccination titers were collected two weeks after vaccination. All cows delivered a live, healthy calf. Samples for BVDV serology and virus isolation were collected from the calves at birth, prior to colostrum intake, and again at 36-48 hours of age. Samples for BVDV serology and virus isolation, and a colostrum sample were collected from the cows prior to the calf suckling. One of the calves from the nonvaccinate group had BVDV present at birth on virus isolation. This was confirmed at necropsy 3 months later. All cows had high titers both pre- and post-vaccination. Colostrum titers for BVDV from all cows were high. Variable BVDV titers were found in the calves. The statistical analysis is not complete, but will be prior to presentation.

Evaluation of Type II Killed BVD Vaccine in the Face of Type II BVD Challenge

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Type II BVD continues to be a concern for cattle producers. Type I MLV BVD vaccines reportedly provide adequate protection against disease caused by Type II BVD. However, MLV vaccines cannot be used in all management situations. This study was designed to test the efficacy of an experimental killed Type II BVD vaccine. In addition, the study compared results with efficacy of modified live and killed Type I BVD vaccines, as well as with efficacy of a killed Type II/MLV Type I combination.

Cattle (n=30) that were seronegative against BVD (SN<1:2) were divided into five test groups of six animals each. On days 0 and 14, cattle were bled and vaccinated with one of the following preparations: **1)** MLV Type I BVD vaccine. This vaccine was prepared according to the current outline of production for MLV BVD vaccine. Product was reconstituted and administered according to the label directions at the time of use. **2)** Killed Type I BVD vaccine. This vaccine was prepared according to the current outline of production for KBVD vaccine. Product was administered according to the label directions. **3)** Killed Type II BVD vaccine. This vaccine was prepared and formulated according to the current outline of production for KBVD vaccine **except** that Type II BVD Strain 125 (NVSL, Ames, Iowa) was used in place of strain C24V. 9CFR final product release tests were performed on the final product. Animals were inoculated with 2 ml of the preparation containing no less than 6.5 logs of Type II Killed BVD virus per dose. **4)** Killed Type I BVD/MLV Type II BVD vaccine. MLV Type I BVD vaccine was reconstituted with the killed type II BVD vaccine described in 3). **5)** RPMI 1640 (untreated control).

Calves were bled on days 21 and on day of challenge. Calves from each group were challenged with Type II BVD (BVD CHV, "890" 94-9, 11/94, NVSL, Ames, Iowa) according to the NVSL Type II challenge protocol on day 28. After challenge, animals were observed daily. Daily rectal temperatures were obtained and clinical signs were scored according to the Diamond Animal Health Carlisle Research Facility scoring key. Daily nasal swabs were taken for virus isolation. Additional serum samples were collected 7 and 14 days after challenge. All serum samples were assayed for the presence of both Type I and Type II BVD-neutralizing antibodies.

Data from clinical scores, viral shedding and serum neutralization studies were statistically evaluated to determine the relative efficacies of the different vaccines. Results showed that the killed Type II, the MLV Type I, and the killed Type II/MLV Type I combination vaccines were effective in protecting calves from Type II BVD challenge, while the killed Type I vaccine was not. Serum neutralization titers suggested that the killed Type II vaccine might confer longer duration of immunity than the MLV Type I vaccine.