Southeast Milk, Inc. Dairy Check-Off Report

Is Testing Cows for Disease Resistance a Practical Tool for Managing Health in Dairy Cows?

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Periparturient immune suppression is well documented and believed to be at least partially responsible for the increased risk of disease during this period. Several studies have found significant differences in immune responsiveness and resistance to disease with alterations in class I and II MHC haplotypes and gene alleles. Other studies have compared incidence of disease among cows categorized based on their antibody mediated immune responsiveness (AMIR) to a novel antigen.

Wagter et al. (2000) were able to quantify and then categorize an individual dairy cow's antibody mediated immune responsiveness (AMIR) to ovalbumin (OVA). High responders for AMIR had the lowest incidence of mastitis in two of the three study herds; with 136 cows and heifers spread over three herds, they were unable to find results that were statistically significant.

The objectives of our study are to categorize cows based on 1) AMIR to OVA and 2) cellular mediated immune response using delayed type hypersensitivity (DTH) reaction to a novel antigen. We then tested for associations between AMIR/CMIR and disease incidence (namely; mastitis, metritis, retained fetal membrane, ketosis, and displaced abomasums), and reproductive efficiency and milk yield.

All test animals were from a single herd in north central Florida which maintains exceptional record keeping. In total, 875 Holstein cows/heifers in good health with no obvious signs of disease were enrolled into the study at 8 weeks (wk-8) prior to expected calving. Animals were enrolled if reconfirmed pregnant with expected dry period less than 90 days.

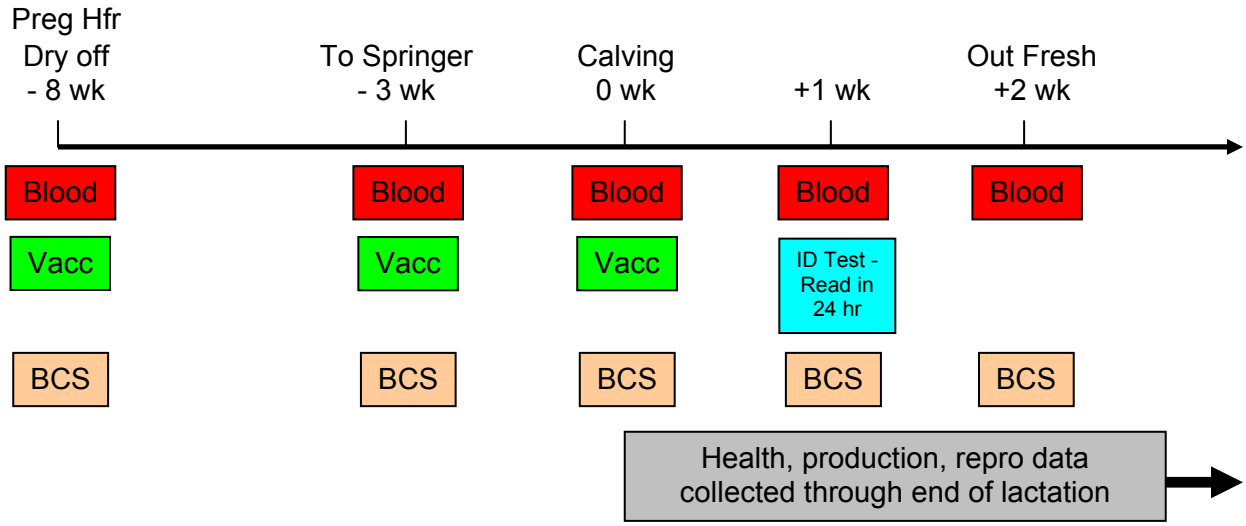

Figure 1 – Schematic of experimental design of a study to determine the association between immune response and clinical disease, reproduction and culling

A schematic of the experimental design is presented in Figure 1. Briefly, test antigens are injected, blood samples collected for antibody titer and body condition scores measured at study enrolment (wk-8), 3 weeks prior to expected calving, at calving and 2 weeks post-calving. Cell mediated immune function was measured at 1 week post-calving. Animals were removed from the study if any data were missing, and if any interval between sampling was less than 12 days. A preliminary analysis was also used to remove an additional 38 animals found not naïve to test antigen. This results in a sample size of 774 with 433 cows and 341 heifers.

Ovalbumin (OVA) was chosen as the antigen to be measured for AMIR due to its inert properties, its ability to stimulate a humoral response, a cow's reduced likelihood of previous exposure and it's previous success as a tool to categorize AMIR. A novel, proprietary antigen was also incorporated into this vaccine to test CMIR.

At 1 week post-calving (wk+1), double skin-fold measurements were taken on the right and left skin folds under the base of the tail using a spring-loaded caliper. The locations of the two measurements were cleaned with 70% isopropyl alcohol. The right side received an intradermal injection of 0.1 mg of novel antigen suspended in 0.1 ml PBS. The left tail fold (control side) received 0.1 ml PBS intradermally. All injections were given with a 28 gauge needle. The exact location of the measurement and injection was marginated with white latex paint. Twenty-four hours later, these injection sites were measured once again to determine the increase in double skin-fold thickness for the right and left side as an indicator for the magnitude of the DTH (CMIR) response.

A cow's specific antibody response to OVA was detected using indirect enzyme-linked immunosorbent assay (ELISA) methods previously described. Some cows developed very high antibody response after the first vaccination (wk-8) and did not have any

further increase in antibody titer; this is termed antibody saturation. Other cows became sick between calving and the wk+2 sampling. T account for these phenomena, an index was generated for the categorization of AMIR.

$$y_{total} = OD_{-3} + OD_0 *(1 + I_2)$$

Where: y_{total} = total antibody
OD_{-3} = optical density value at wk-3
OD_0 = optical density value at wk0
I_2 = change in OD between week -3 and week 0

The y_{total} values within parity were then ranked high to low. Cows within the bottom 25% for a respective parity are categorized as low AMIR responders, while cows in the top 25% for a respective parity are termed high AMIR responders. The remaining middle 50% are categorized as medium AMIR responders.

A normal distribution was required for the determination of CMIR categorization; so as a result, log transformations of the measurements were performed. The magnitude of the DTH response was determined by the following:

$$y = \ln(R24) - \ln(R0) \quad (5\text{-}1)$$

To extrapolate CMIR categorizations the mean and standard deviation for the "y" values were configured for all cows respective of parity. Cows with "y" values above the mean plus one standard deviation were classified as high CMIR responders. Those cows below one standard deviation less than the mean were classified as low CMIR responders. All animals within one standard deviation of the mean were medium responders.

Identification of disease was performed by farm personnel who were blinded to immune response categorizations. The diseases of interest for this project were; mastitis, metritis, retained fetal membrane, ketosis, and displaced abomasum. All diseases were recorded as yes/no binary responses for the trial period of the current lactation.

Milk yield and reproductive data were gathered from the Dairy Herd Information Association (DHIA) records for the current lactation. Appropriate statistical analyses were performed using SAS. Statistical significance was determined at $p < 0.05$.

Antibody mediated immune response category was associated with occurrence of mastitis and ketosis. High responders had less mastitis and ketosis than medium or lower responders. High AMIR category was also negatively associated with milk yield ($p=0.06$) and pregnancy rate at 150 days in milk ($P<0.05$). Increased risk of mastitis was also noted in medium CMIR responders compared with high CMIR responders ($P<0.05$). Of particular note was the association between CMIR categories and occurrence of RFM. High responders had significantly lower risk of RFM than either medium or low responders. CMIR response was also associated with milk yield (p =

0.049, β = 508.08). CMIR was not a significant predictor for pregnancy by 150 DIM (p = 0.77).

Immune response, either humoral (AMIR) or cellular was associated with some diseases of dairy cattle. AMIR tended to be inversely related with CMIR. High AMIR responders appeared to have lower milk production and took longer to get pregnant. These phenomena could not be explained by this study. Some hypothesize that in high immune responders, more nutrients are required to manage the highly active immune system and less is available for production. Since pregnancy is dependent on the conceptus avoiding the maternal immune system, the highly active immune system of high responders may overwhelm this system resulting in lower conception rates.

Notes