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Short communication: Variation in production parameters among Canadian Holstein cows classified as high, average, and low immune responders

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ABSTRACT

Dairy cattle evaluated for immune responses and identified as high responders are known to have a lower occurrence of economically important diseases, including mastitis, metritis, ketosis, and retained placenta. These high immune responders have also been shown to make more antibody following vaccination and to have improved milk and colostrum quality. Therefore, breeding for improved immune response is expected to have several benefits in the dairy industry. However, a concern of such an approach to improve animal health is the potential cost of lost production due to an allocation of host resources to mount a robust immune response. The objective of this study was to evaluate early- and late-lactation production parameters in cattle classified as having high, average, or low estimated breeding values (EBV) for cell-mediated (CMIR), antibody-mediated (AMIR), and overall immune responses. A total of 561 cows from 6 herds were phenotyped for immune response and ranked based on EBV for CMIR and AMIR. A linear animal model was used to evaluate differences in milk, fat, and protein yields among immune response groups, and a regression analysis was conducted based on immune response EBV. Overall, no difference in production parameters was found based on immune response rank; however, some positive relationships with immune response EBV were found, suggesting that breeding for enhanced immune responsiveness as a prophylactic approach to improve animal health would not come at the cost of lost production.

Key words: dairy cattle, immune response, milk, production

Short Communication

Although substantial genetic advancements are being made along with increasing milk production in the dairy industry, disease occurrence continues to be a prevalent problem as it incurs costs to both the producer and consumer (Oltenacu and Broom, 2010). A proposed solution to decrease disease is the incorporation of immune response (**IR**) traits into current selection indices to breed for broad-based disease resistance (Wilkie and Mallard, 1999; Abdel-Azim et al., 2005). The adaptive immune response phenotype can be evaluated using a patented protocol (US#7,258,858; Wagter-Lesperance and Mallard, 2007), allowing cows to be selected on both cell-mediated immune response (**CMIR**) and antibody-mediated immune response (**AMIR**) for an overall high immune response profile.

Various components allow the immune system to mount both innate responses, along with more specific adaptive responses (Kumar and Burns, 2008). The adaptive immune system is mediated by cells and cytokines and can be broadly categorized into CMIR and AMIR; it is capable of memory and mounting a superior response to subsequent exposure of an antigen through the proliferation of memory B and T cells (Ingvartsen et al., 2003; Crawley et al., 2005; Lippolis, 2008). The CMIR targets intracellular pathogens such as viruses and *Mycobacterium avium* ssp. *paratuberculosis*, which causes Johne's disease in dairy cattle (Koo et al., 2004). On the other hand, the AMIR targets extracellular pathogens, including mastitis-causing bacteria, through the production of antibodies (Thompson-Crispi et al., 2012b).

Multiple studies have shown that high-immune-responding (HIR) dairy cattle have a lower occurrence of infectious and metabolic diseases such as mastitis, metritis, ketosis, and retained fetal membranes (De La Paz, 2008; Thompson-Crispi et al., 2012a, 2013), along with better response to vaccines and higher milk and colostrum quality (Wagter et al., 2000; Fleming, 2014). Overall, breeding for immune response is expected to reduce disease and improve animal health and well-being (Thompson-Crispi et al., 2014; Mallard et al., 2015). Furthermore, immune response traits are heritable, with recent estimates of 0.29 and 0.19 for AMIR and CMIR, respectively, indicating that genetic progress is possible (Thompson-Crispi et al., 2012b).

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A previous study that classified animals based solely on their antibody response demonstrated no adverse effects on 305-d milk yield. Wagter et al. (2003) observed higher fat and protein yields in low-responder, first-parity cows compared with average or high responders when ranked based on AMIR; however, these differences for protein and fat did not carry over into older cows. Additionally, the high-AMIR cows in third or greater parity had a higher milk yield than the average and low groups (Wagter et al., 2003). Another study examined correlations of sire EBV for AMIR and CMIR with 45 traits from the lifetime profit index. Of the production traits, significant correlations were observed only between AMIR and milk fat (0.184; $P = 0.011$) and CMIR and milk protein (−0.147; $P = 0.042$) (Heriazon et al., 2013). On the other hand, positive genetic correlations for CMIR with milk yield have been reported at 0.16 ($P \leq 0.01$) (Thompson-Crispi et al., 2012b). These previous studies used 305-d projected milk, fat, and protein yields; however, associations with early-lactation production parameters remain unknown. The objectives of this study were to (1) use standardized breeding values to classify cattle as high, average, or low immune responders for CMIR, AMIR, and overall IR; (2) evaluate the association of AMIR, CMIR, and overall IR rank with milk and production parameters from the first 60 DIM; and (3) evaluate the association of AMIR, CMIR, and overall IR with complete 305-d production records.

All experimental procedures were approved by the Animal Care Committee of the University of Guelph under guidelines of the Canadian Council of Animal Care (1993). A total of 561 Holstein cows and heifers from 6 commercial herds in southern Ontario were evaluated for immune response using the patented HIR test protocol (Wagter-Lesperance and Mallard, 2007). Briefly, all cattle were immunized intramuscularly on d 0 (study start day) with 0.5 mg of type-I antigen, 0.5 mg of type-II antigen, and 0.5 mg of Quil-A adjuvant (Cedarlane Laboratories Ltd., Hornby, ON, Canada) dissolved in 1.0 mL of PBS. A blood sample was taken on d 0 as a measure of baseline antibody response and at d 14 to measure a primary antibody response. A delayed-type hypersensitivity (DTH) to the type-I antigen and a PBS control was used as a measure of CMIR and was initiated at d 14 postimmunization (Hernández et al., 2005; Heriazon et al., 2009). Skin thickness measurements were taken on both tail folds, and cows then received an intradermal injection of the type-I antigen on the right tail fold and a PBS control on the left tail fold. Twenty-four hours later, skin thickness measurements were repeated. The ratio of skin thickness measurements at 24 h to 0 h relative to intradermal injection was used for both the test site and control sites. The AMIR was evaluated by antibody production in response to the type-II antigen (Heriazon et al., 2009). Serum antibody was quantified using a modified ELISA protocol as described by Hine et al. (2011) from blood collected on d 0 and 14 of the test protocol.

Complete immune response phenotypes and registration numbers were available for 561 dairy cattle from 6 herds (herd 1, n = 112; herd 2, n = 60; herd 3, n = 94; herd 4, n = 118; herd 5, n = 95; herd 6, n = 82). The full pedigree included 26,673 animals and was provided by the Canadian Dairy Network (Guelph, Ontario). For CMIR, the response variable was the log ratio of the 24-h skin thickness measurement at the test site to the 0-h test site measurement, with the control site as a covariate. For AMIR, the d 14 value, indicative of a primary antibody response, was the response variable and the d 0 value was the covariate. ASREML software (Gilmour et al., 1995) was used to estimate heritability and breeding values to rank animals for CMIR or AMIR based on the following univariate linear animal model:

$$y_{ijklmn} = \mu + \alpha \times d_i + h_j + p_k + sl_l + ps_m + a_n + e_{ijklmn},$$

where y_{ijklmn} = CMIR or AMIR; μ = population mean; d_i = control site of CMIR or AMIR at d-0 as fixed regressions; α is a regression coefficient; h_j = fixed effect of herd (1–6); p_k = fixed effect of parity (0, 1, 2, 3, ≥4); sl_l = fixed effect of stage of lactation group (not lactating, 1–20, 21–105, 106–235, >235 DIM); ps_m = fixed effect of pregnancy status (not pregnant, <100, 100–200, >200 d pregnant); a_n = random animal effect; and e_{ijklmn} = residual error. Variables with $P > 0.1$ were removed from the model and results were considered to be statistically significant if $P \leq 0.05$. Interactions were tested and remained in the model if $P < 0.1$. The EBV were standardized to a mean of 0 and a standard deviation of 1; animals with an EBV ≥ +1 standard deviation (**SD**) from the mean were classified as high responders, those with an EBV ≤ −1 SD were classified as low immune responders, and those with an EBV between −1 and +1 SD from the mean were average immune responders. To have an EBV for overall IR, standardized breeding values for CMIR and AMIR were averaged as described previously (Thompson-Crispi et al., 2012b).

Milk records within the first 60 DIM of lactation were available for 442 of the tested animals, and complete 305-d records for 402 cows, through the Ontario Dairy Herd Improvement Corporation and the Canadian Dairy Network. Records were obtained from the lactation in which animals were IR tested, or in the