A METHOD FOR DEVELOPING A BREEDING OBJECTIVE TRAIT FROM MULTIPLE COMPONENTS USING THE EXAMPLE OF IMMUNE COMPETENCE IN AUSTRALIAN ANGUS CATTLE

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SUMMARY

Traits that are being recorded in livestock improvement programs might not be suitable breeding objective traits themselves, which is an important aspect for the consideration of novel traits in breeding programs. Here we demonstrate, using the example of immune competence in cattle, how multiple novel traits can be reduced to a single breeding objective trait. It was demonstrated that it is possible to achieve a high heritability for the novel single breeding objective trait and maximise the genetic correlation with one of the major production traits, here final weight. An approach as described here would maximise the genetic gain in the novel trait.

INTRODUCTION

In order to respond to future livestock industry needs, novel traits are being developed to promote sustainable livestock production. One such desirable attribute of the animal is immune competence (IC) (Wilkie *et al.* 1999), which has demonstrated health benefits in dairy cattle (Thompson-Crispi *et al.* 2012; Aleri *et al.* 2019). A protocol for measuring IC has been developed in Australian Angus Cattle (Hine *et al.* 2019). Immune competence has two components: cell-mediated (Cell-IR) and antibody-mediated immune responses (Ab-IR). These represent two aspects of adaptive immune responses that help control infectious disease. However, in a breeding objective context, it would be easier to use immune competence, as a combination of Ab-IR and Cell-IR, as a single breeding objective trait. The aim of this study was to combine the two immune response traits into a single breeding objective trait, here IC, so that the heritability for IC is high and the correlation of IC with final weight (FW), one of the key profit drivers, is maximised to allow for the highest possible genetic gain in the novel trait through direct and correlated response.

MATERIALS AND METHODS

Data. A protocol has been developed to measure Cell-IR and Ab-IR in commercial beef herds (Hine *et al.* 2019). Immune response phenotypes were recorded on 1,149 Angus cattle from the Angus Sire Benchmarking Program. Animals originated from five different herds and were born across three years. Link sires were used to provide connections between herds and birth cohorts. Not all animals within a herd could be tested in one day, and up to 7 test cohorts exist within a herd. Immune response phenotypes were assessed during the yard weaning period. On the day of weaning (Day 0) cattle were vaccinated with a multi-valent clostridial vaccine containing tetanus toxoid antigen (Zoetis, Australia). The ability to mount an Ab-IR was measured as production of tetanus toxoid specific IgG1 antibody in blood between day 8 and day 21 post-vaccination. The actual sampling day was dependent on the specific herd and their prior clostridial vaccination history. Vaccination history was identical for animals tested within herd and test cohort. The antibody concentration measured in blood represents a cumulative response to the vaccination given at day 0 and to any vaccinations

administered previously. An in-house indirect ELISA method was used to measure antibody levels (Aleri *et al.* 2015). The Ab-IR was recorded as optical density values (OD) and for analysis the OD values were square root transformed.

Cell-mediated immune response (Cell-IR) was assessed as delayed type hypersensitivity (DTH) by measuring changes in skin fold thickness in response to intradermal injection of the clostridial vaccine (Ultravac 7 in 1 clostridial and leptospira vaccine (Zoetis)) in the caudal fold of the tail. Testing day was consistent within herd and test cohort and was conducted around day 14 post vaccination aligning with blood collection for antibody testing. One side of the tail was injected with 100 µL of Ultravac 7 in 1 (test) and the other with 100 µL of saline (control). Skin thickness was measured in millimetres using callipers prior to injection (T0) and after 48 hours (T48). The magnitude of DTH responses was determined as the T48 test response in relation to the T48 control response (DTH T48 test/DTH T48 control). The DTH response at T0 (DTH T0 test/DTH T0 control) was fitted as a covariate in the linear model. The Cell-IR variable and covariate were log transformed prior to analysis to ensure normality.

The two immune response traits, Cell-IR and Ab-IR, were both multiplied by 100 for analysis. Cattle were finished through a feedlot after backgrounding at pasture for approximately nine months and final weight, the weight when animals were sent to the feedlot at approximately 600 days (FW), was also used for analysis. Fixed effects included contemporary group (herd, birth year, test cohort) for all traits. For Cell-IR and Ab-IR, age at testing was fitted as a covariate. Age at the measurement of FW was fitted as covariate for FW. To prove the hypothesis, this study only animals with all data for phenotypes, fixed effects and covariates were included in the study, which resulted in a data set with 851 animals (all male) and 2,128 animals in the pedigree.

Analysis. Variance components and heritabilities were estimated using VCE 6.0.2 (Kovac *et al.* 2010) and genetic and phenotypic correlations were estimated for FW, Cell-IR and Ab-IR. Here we explored whether the two immune response traits could be combined into a single IC trait as the relevant single breeding objective trait in a breeding program. The hypothesis was that the two traits could be combined such that the heritability for IC is high and the correlation between IC with FW is most strongly negative. This is not a realistic example as we would not attempt to maximise an unfavourable correlation, but the data set offered the highest number of records for FW and a strong correlation with IC, which helps to prove the hypothesis. Immune competence was calculated using the following function: $IC = \alpha \times \text{Cell-IR} + (1- \alpha) \times \text{Ab-IR}$, with $\alpha = 0$ to 1. For each α, ranging from 0 to 1, a bivariate analysis was run for IC and FW. Breeding values (EBV) and heritabilities were estimated for IC along with genetic correlations between IC and FW.

RESULTS AND DISCUSSION

The summary statistics for immune response and FW traits are shown in Table 1. The amount of phenotypic variation in the immune response traits was expected since they have not been traits of direct selection. However, at this point there are no results how that variation relates to variation in disease protection. The negative minimum of Cell-IR indicates that in some animals the skin thickness after challenge reduced compared to Day 0 as is seen in other studies. Final weights ranged from 476kg to 880kg across contemporary groups/properties. Within properties there is much less variation, highlighting the need to fit contemporary group.

Table 1. Descriptive statistics of cell-mediated and antibody-mediated immune response (Cell-IR and Ab-IR, multiplied by 100) and final weight (kg)

	Minimum	Maximum	Mean ± Standard deviation
Cell-IR*	-2.30	56.08	24.22 ± 9.01
Ab-IR*	14.90	143.26	78.36 ± 25.08
FW	476.00	880.00	559.87 ± 88.37

*Cell-IR was log transformed and Ab-IR square root transformed

Heritabilities for Cell-IR and Ab-IR were moderate (Table 2) and are in line with previous estimates from all 1,149 animals (Hine *et al.* 2019). The genetic correlation between the immune response traits was moderately positive, which confirmed previous estimates from the full data set (Hine *et al.* 2019). Genetic correlations of Cell-IR and Ab-IR with FW are negative, possibly indicating that high immune response diverts energy resources from growth.

Table 2. Heritabilities (diagonal, bold) and genetic correlations (below diagonal)

	Cell-IR	Ab-IR	FW
Cell-IR	**0.33 ± 0.11**		
Ab-IR	0.40 ± 0.22	**0.30 ± 0.10**	
FW	-0.27 ± 0.21	-0.50 ± 0.19	0.48 ± 0.12

Table 3 outlines the results from the bivariate analyses of IC and FW, where IC is a function of the weighted component traits Cell-IR and Ab-IR. At α = 0.0 IC is the same as Ab-IR, at α = 1.0 IC is the same as Cell-IR. The heritability of IC is moderate and the genetic correlation with FW is most strongly negative at α = 0.3. Genetic gains for IC could be maximised through selection on IC and the highly correlated trait FW, however, because the correlation is negative, FW would be reduced. Alternatively, at α = 1.0, the negative correlation with FW would be minimised, but would result in IC being only a representation of Cell-IR.

Table 3. Heritability of immune competence (IC) and genetic correlation with final weight (FW) at different weightings (α) to combine cell-mediated and antibody-mediated immune response traits; standard errors (se) in brackets

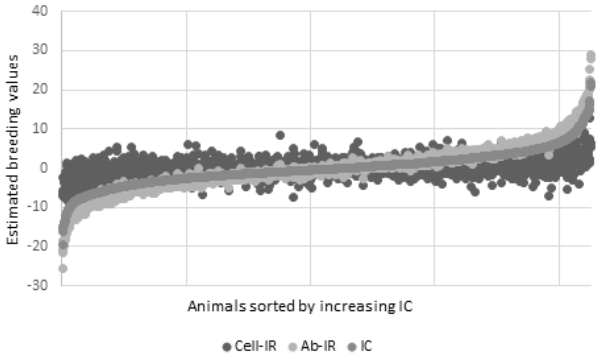
α	h^2IC (se)	r_g (se)
0.0	0.299 (0.107)	-0.500 (0.223)
0.1	0.306 (0.106)	-0.503 (0.210)
0.2	0.315 (0.103)	-0.505 (0.214)
0.3	0.325 (0.111)	-0.506 (0.198)
0.4	0.338 (0.111)	-0.505 (0.206)
0.5	0.354 (0.114)	-0.500 (0.195)
0.6	0.371 (0.112)	-0.488 (0.206)
0.7	0.384 (0.114)	-0.465 (0.193)
0.8	0.384 (0.116)	-0.425 (0.207)
0.9	0.362 (0.119)	-0.362 (0.211)
1.0	0.322 (0.109)	-0.274 (0.210)

Figure 1 shows, animals can be differentiated based on the EBV for IC. As can be expected at **α**=0.3, EBV for IC are a closer reflection of the EBV for Ab-IR than for Cell-IR. Ideally, animals

with high EBV for IC would reflect high EBV for both Ab-IR and Cell-IR, because both types of responses are required to effectively control environmental pathogens. In addition to the approach presented here, other ways to define IC as breeding objective trait to allow equal emphasis on both component traits of IC need to be explored.

Results using the example of IC are instructive. The small amount of variation observed in r_g for values of **α** between 0.1 and 0.6 suggest that for this trait there is considerable latitude to vary weighting on Ab-IR and Cell-IR with little variation in the penalty to FW. Ab-IR and Cell-IR also influence other drivers of profitability (Hine *et al.* 2016), highlighting the need for a more comprehensive method for incorporating Ab-IR and Cell-IR as the novel multi-component trait IC.

Figure 1. Estimated breeding values for Cell-IR, Ab-IR and IC at α=0.3, sorted from highest to lowest IC EBV



CONCLUSION

Novel traits provide an opportunity to extend traditional livestock breeding objectives to ensure the industry's future sustainability. Strategically defining the breeding objective trait can assist in incorporating novel trait in breeding programs.

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