IMMUNE COMPETENCE AND MICRO-ENVIRONMENTAL SENSITIVITY

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SUMMARY

The aim of this study was to estimate the genetic relationship between immune competence and micro-environmental sensitivity (ES) of weaning weight, eye muscle area, and rib and rump fat depth. Variation in micro-environmental sensitivity among livestock leads to variability of phenotypes. The genetic correlations indicated that animals with higher immune competence tended to have lower micro-ES of weaning weight and eye muscle area, and higher micro-ES of rib and rump fat depth.

INTRODUCTION

Selecting to improve the immune competence (IC) of livestock could potentially lead to increased health and welfare of the animals, and decrease the livestock industry's reliance on antibiotics (Dominik *et al.* 2019; Hine *et al.* 2019; Hine *et al.* 2021; Reverter *et al.* 2021a; Reverter *et al.* 2021b). Furthermore, improved immunity could reduce the production loss and cost of medical intervention associated with disease incidences thus increasing profits (Hine *et al.* 2021).

The immune system is a complex system affecting many other systems in the animals, which can influence many phenotypes. The relationship between IC and live weight traits, growth and eye muscle area have been found to be unfavourable, while carcass traits and dry matter intake have a less straight forward relationship with IC (Reverter *et al.* 2021b). Aside from the direct relationship between IC and production traits, it is possible the IC affects the variability of production traits. The variability of phenotypes can vary between animals of different genetic backgrounds, in which case the genotypes exhibit micro-environmental sensitivity (micro-ES). Animals with less micro-ES are expected to respond less to disturbances in their environments and can be quantified at a genetic heterogeneity of the environmental variance (SanCristobal-Gaudy *et al.* 1998; Hill and Mulder 2010). The relationship between IC and micro-ES has not yet been reported.

The aim of this study was to investigate the relationship between IC and some production traits and between IC and the micro-ES of production traits in Australian Angus cattle.

MATERIALS AND METHODS

Data. Antibody- and cell-mediated immune response (AMIR, CMIR) were the IC component traits. The AMIR and CMIR records were provided by CSIRO and Angus Australia. The records were collected in 2012-2020 in accordance with the procedures described by Hine *et al.* (2019). The AMIR phenotypic values represent the level of antigen-specific serum IgG1 antibody in response to vaccination with Ultravac 7in1 vaccine (Zoetis) and were calculated from the square root transformed optical density values generated using an enzyme-linked immunosorbent assay and corrected for inter-plate variation. The CMIR phenotypes were calculated from the log-transformed ratio between the measured double skinfold thickness at test (intradermal vaccine injection) and control site (intradermal saline injection) (Hine et al. 2019). To account for initial double skinfold thickness, the pre-injection log-transformed ratio between the double skinfold thickness at test and control site was used as a covariate in the analysis.

Production traits consisted of weaning weight (WW), scan eye muscle area (EMA), scan rib fat depth (RIB) and scan rump fat depth (P8). The production traits were provided by Angus Australia and were part of the routine recording scheme between 2012 and 2020.

For the IC records, contemporary groups (CG) were constructed by concatenating herd, year and test cohort. For the production traits, trait specific CGs were concatenations of herd, birth year, observation date for the trait, breeder defined management group, birth type and embryo transfer status. Age slicing further subdivided CGs for WW, RIB, P8 and EMA. Age slices covered 45 days for WW and 60 days for RIB, P8 and EMA as per Graser *et al.* (2005), and slices were symmetric around the average age of the CG. Summary statistics are shown in Table 1. Two pedigrees were used for analysis, one for sire (10948 animals) and one for rearing dams (98151 animals).

Table 1. Summary statistics for the final dataset

Parameter	Statistic	WW (kg)	RIB (mm)	P8 (mm)	EMA (cm^2)	AMIR	CMIR
Records	Count	31699	83034	83314	83486	3910	3908
Phenotype	Mean	254.60	6.11	7.89	80.49	0.85	1.89
	SD	51.63	2.76	3.73	17.56	0.43	0.42
	Range	77-496	1-22	1-33	31-157	0.01-2.13	0.85-4.92

Analysis. The data was analysed using 8 two-trait models with an IC trait as one trait and a production trait as the second trait. The production traits were fitted with a double hierarchical generalised linear model (DHGLM) for estimating the micro-ES of the production traits resulting in a trivariate model. The general model was:

$$\begin{bmatrix} \boldsymbol{y_{IC}} \\ \boldsymbol{y_{PT}} \\ \boldsymbol{y_{mES}} \end{bmatrix} = \begin{bmatrix} \boldsymbol{X_{IC}} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{X_{PT}} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{X_{mES}} \end{bmatrix} \begin{bmatrix} \boldsymbol{b_{IC}} \\ \boldsymbol{b_{PT}} \\ \boldsymbol{b_{mES}} \end{bmatrix} + \begin{bmatrix} \boldsymbol{Z_{IC}} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{Z_{PT}} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{Z_{mES}} \end{bmatrix} \begin{bmatrix} \boldsymbol{s_{IC}} \\ \boldsymbol{s_{PT}} \\ \boldsymbol{s_{mES}} \end{bmatrix} + \begin{bmatrix} \boldsymbol{e_{IC}} \\ \boldsymbol{e_{PT}} \\ \boldsymbol{e_{mES}} \end{bmatrix}$$

where $\boldsymbol{y_{IC}}$, $\boldsymbol{y_{PT}}$ and $\boldsymbol{y_{mES}}$ were the IC trait (AMIR or CMIR), the production trait phenotype and calculated micro-ES phenotype of the production trait, respectively. $\boldsymbol{b_{IC}}$ contained the fixed effects of sex and CG for AMIR and the fixed effect of CG and the pre-injection covariate for CMIR, $\boldsymbol{b_{PT}}$ and $\boldsymbol{b_{mES}}$ contained the fixed effects of sex and CG and covariate of age for the production traits (and the covariate of dam age and squared dam age for WW). $\boldsymbol{s_x}$ and $\boldsymbol{e_x}$ were the fixed effects, additive genetic sire effects and residuals of trait x ($x \in (IC,\ PT, mES)$). The micro-ES phenotype was calculated as $\boldsymbol{y_{mES}} = \hat{\boldsymbol{e}}^{\boldsymbol{2}}_{\boldsymbol{PT}} /(\boldsymbol{1} - \boldsymbol{h_{PT}})$, where $\boldsymbol{h}_{\mathbf{PT}}$ was the diagonal element of the part of the hat-matrix corresponding to $\boldsymbol{y}_{\mathrm{PT}}$ ($\hat{\boldsymbol{y}}_{\boldsymbol{PT}} = \boldsymbol{H}\boldsymbol{y_{PT}}$) also known as the leverage (Hoaglin and Welsch 1978). For models where WW was the production trait, the model also included maternal genetic ($\boldsymbol{c}$) and permanent environmental ($\boldsymbol{pe}$) effects.

The distribution assumptions for the random genetic sire effects were $\begin{bmatrix} \boldsymbol{s_{IC}} \\ \boldsymbol{s_{PT}} \\ \boldsymbol{s_{mES}} \end{bmatrix} \sim MVN\left(\begin{bmatrix} \boldsymbol{0} \\ \boldsymbol{0} \\ \boldsymbol{0} \end{bmatrix}, \begin{bmatrix} \sigma^2_{s_{IC}} & \sigma_{s_{IC}s_{PT}} & \sigma_{s_{IC}s_{mES}} \\ & \sigma^2_{s_{PT}} & \sigma_{s_{m}s_{mES}} \\ & & \sigma^2_{s_{mES}} \end{bmatrix} \otimes \boldsymbol{A}\right)$, where $\boldsymbol{A}$ was the numerator relationship matrix among sires based on the sire pedigree and $\otimes$ is the Kronecker product. The distribution assumptions of the residuals were $\begin{bmatrix} \boldsymbol{e_{IC}} \\ \boldsymbol{e_{PT}} \\ \boldsymbol{e_{mES}} \end{bmatrix} \sim MVN\left(\begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \boldsymbol{I}\sigma^2_{e_{IC}} & 0 & 0 \\ 0 & \boldsymbol{W^{-1}_{PT}}\sigma^2_{\epsilon_{PT}} & 0 \\ 0 & 0 & \boldsymbol{W^{-1}_{mES}}\sigma^2_{\epsilon_{mES}} \end{bmatrix}\right)$, where $\boldsymbol{I}$ was an identity matrix of appropriate size, and $\boldsymbol{W_{PT}}$ and $\boldsymbol{W_{mES}}$ were matrices containing weights

for the residual variances of the DHGLM. $\boldsymbol{W_{PT}} = diag(\widehat{\boldsymbol{y_{mES}}})^{-1}$ and $\boldsymbol{W_{mES}} = diag((1 - \boldsymbol{h_{PT}})/2)$.

Post analysis corrections of variance components to obtain additive genetic and residual variances on the animal level were applied as described in Madsen *et al.* (2021). The variation and heritability of micro-ES ($h^{2^*}_{mES}$) was converted from the logarithmic to the measurement level following Mulder *et al.* (2007) and Mulder *et al.* (2009).

RESULTS AND DISCUSSION

The results showed additive genetic variance of micro-ES in all production traits (Table 2). The heritabilities were in line with the heritabilities reported for production traits in Nellore beef cattle by Neves *et al.* (2011) and Iung *et al.* (2017). The genetic coefficient of variation (GCV) of micro-ES was low to moderate, with higher values for the fat traits. The higher GCV of RIB and P8 indicate that some response to selection could be obtained.

The heritability of AMIR and CMIR were in line with those previously reported (Dominik *et al.* 2019; Hine *et al.* 2019; Reverter *et al.* 2021a; Reverter *et al.* 2021b). Likewise, the heritabilities of EMA and P8 were within previously reported values for Australian beef cattle, while the heritability of RIB was slightly higher than previously reported (Meyer *et al.* 2004; Jeyaruban *et al.* 2009). In contrast, the heritability of WW was higher than the 0.13-0.35 reported for Australian beef cattle (Meyer *et al.* 2004; Jeyaruban *et al.* 2009; Torres-Vázquez *et al.* 2018). Slightly larger heritabilities can be expected when a trait is fitted with a DHGLM as the genetic variation due to micro-ES is removed from the observed residual variance of the phenotype reducing the denominator used to calculate the heritability.

Table 2. Estimated heritabilities and genetic coefficient of variation

	AMIR	**CMIR**	**WW**	**RIB**	**P8**	**EMA**
$\boldsymbol{h^2}$ (%)	36.18	35.62	43.50	34.58	35.11	25.13
$\boldsymbol{h^{2^*}_{mES}}$(%)			0.03	1.22	1.42	0.35
$\boldsymbol{GCV_{mES}}$ (%)			13	24	27	11

Table 3. Genetic correlations between the production and immune traits in Angus cattle*

	AMIR			**CMIR**		
	$r_{AMIR,PT}$	$r_{AMIR,mES}$	$r_{PT,mES}$	$r_{CMIR,PT}$	$r_{CMIR,mES}$	$r_{PT,mES}$
WW	*-0.35*	-0.12	*0.18*	*-0.26*	-0.15	*0.18*
RIB	0.11	0.14	*0.87*	0.15	0.09	*0.87*
P8	0.06	0.00	*0.90*	0.16	0.12	*0.90*
EMA	-0.13	-0.34	*0.30*	0.04	-0.17	*0.31*

*Italic values had 95% confidence intervals not including 0

The genetic correlations between the IC traits and RIB and P8 indicated that animals with higher fatness also tended to have higher IC (Table 3). In contrast, the genetic correlations indicated that animals with higher IC had lower WW, showing that immune response may be utilising resources that would otherwise have contributed towards growth. The genetic correlations between micro-ES of production traits and IC tended to be moderately negative for WW and EMA and non-existing to lowly positive for RIB and P8. The genetic correlations involving the IC traits had large SEs and

therefore only the genetic correlations between WW and either IC trait had a 95% confidence interval not including 0. The larger SEs were likely due to the small data size of the two IC traits.

The genetic correlations between the production traits and their micro-ES were strongly positive for RIB and P8 fat showing that selection to reduce fatness would have a correlated decrease in the micro-ES of fatness and vice versa.

CONCLUSIONS

All production traits showed micro-ES. The heritabilities and genetic coefficient of variance of micro-ES was higher for RIB and P8 than the other production traits. Selection to decrease micro-ES may be possible for these traits.

Results showed that mounting immune responses might direct resources away from growth.

The positive genetic correlation between the fat and IC traits indicated that animals with higher fatness also have higher ICs.

The genetic correlations between the IC traits and micro-ES of production traits showed a tendency for animals with higher genetic potential for IC to have lower micro-ES of WW and EMA and higher micro-ES of RIB and P8.

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