Animal Production Science, 2021, **61**, 1919–1924
https://doi.org/10.1071/AN21054

ImmuneDEX: updated genomic estimates of genetic parameters and breeding values for Australian Angus cattle

Antonio Reverter[A,D], *Brad C. Hine*[B], *Laercio Porto-Neto*[A], *Pamela A. Alexandre*[A], *Yutao Li*[A], *Christian J. Duff*[C], *Sonja Dominik*[B] *and Aaron B. Ingham*[A]

[A]CSIRO Agriculture & Food, Queensland Bioscience Precinct, 306 Carmody Road, St Lucia, Brisbane, Qld 4067, Australia.
[B]CSIRO Agriculture & Food, F.D. McMaster Laboratory, Chiswick, New England Highway, Armidale, NSW 2350, Australia.
[C]Angus Australia, 86 Glen Innes Road, Armidale, NSW 2350, Australia.
[D]Corresponding author. Email: tony.reverter-gomez@csiro.au

Abstract

Context. Immune competence is a proxy trait for general disease resistance and is based on combined measures of an animal's ability to mount both a cell-mediated immune response (Cell-IR) and an antibody-mediated immune response (Ab-IR). On the basis of previously described arithmetic, we combined these measures into a single proxy trait for immune competence, named ImmuneDEX (IDEX).

Aims. Using a population of 3715 Australian Angus steers (n = 2395) and heifers (n = 1320) with genotypes for 45 364 single-nucleotide polymorphisms, we provide the latest genomic estimates of heritability and genetic correlations for IDEX and the components Cell-IR and Ab-IR immune competence phenotypes. Accuracy and bias of genomic predictions of breeding values are also presented and discussed.

Methods. Measures of Cell-IR, Ab-IR and IDEX were analysed jointly in a tri-variate genomic restricted maximum-likelihood model that contained the fixed effects of contemporary group with 80 levels, the linear covariates of age at measurement and change in skin thickness at control site, and the random polygenic (genomic estimated breeding value, GEBV) and residual effects. Following Method LR procedures, we estimate accuracy, bias and dispersion of genomic predictions using a cross-validation scheme based on five year-of-birth cohorts.

Key results. We report genomic restricted maximum-likelihood model estimates of heritability of 0.247 ± 0.040 for Cell-IR, 0.326 ± 0.059 for Ab-IR, 0.275 ± 0.046 for IDEX. While a small positive genetic correlation (r_g) was estimated between Cell-IR and Ab-IR (r_g = 0.138 ± 0.095), strongly positive estimates were obtained between IDEX and Cell-IR (r_g = 0.740 ± 0.044) and between IDEX and Ab-IR (r_g = 0.741 ± 0.036). Averaged across the five validation sets, the accuracy of GEBV for Cell-IR, Ab-IR and IDEX was 0.405, 0.443 and 0.411 respectively. Also, some significant bias or dispersion can be expected depending on the cohort used as the validation population.

Conclusions. Consistent with previous findings, immune competence phenotypes are moderately heritable and accurate GEBV can be generated to allow the selection of cattle with an improved ability to mount a general immune response.

Implications. Our analyses suggest that ImmuneDEX will provide a tool to underpin long-term genetic strategies aimed at improving the immune competence of Australian Angus cattle in production systems, which, in turn, is expected to reduce the incidence of disease and our reliance on antibiotics to treat disease.

Keywords: beef cattle, heritability, immune competence, genomic predictions, accuracy.

Received 5 February 2021, accepted 11 June 2021, published online 17 August 2021

Introduction

The ability to simultaneously select for improved productivity and animal welfare outcomes is key to maintain sustainable livestock production. One way to achieve this goal is to breed animals with enhanced immune competence, described as an animal's ability to mount an immune response, which is expected to be an indirect indicator of an animal's ability to resist disease challenges faced in their production environment (Wilkie and Mallard 1999).

Using a population of 1149 Australian Angus cattle, Hine *et al*. (2019) developed a method for on-farm assessment of immune competence in beef cattle, which combines measures

of an animal's ability to mount both a cell-mediated immune response (Cell-IR) and an antibody-mediated immune response (Ab-IR). Using the same animal resource, Dominik *et al.* (2019) applied a weighted average to combine both immune response metrics into a single immune competence phenotype. Their results suggested that a stronger emphasis on Cell-IR would minimise negative impacts on the production trait, feedlot exit weight; however, the importance of a balanced ability to mount both Cell-IR and Ab-IR for general disease resistance was acknowledged.

More recently, Reverter *et al.* (2021) expanded that earlier work by using a population of 2853 Australian Angus steers and heifers to estimate pedigree-based genetic parameters for immune response metrics. The authors also introduced ImmuneDEX (IDEX) as a single phenotype that describes immune competence by combining Cell-IR and Ab-IR into a single measure and reported its relationship with commonly measured traits related to growth, feedlot performance and carcass characteristics. Key findings for that earlier work indicated that ImmuneDEX will provide a basis to breed animals that are both highly productive and with an enhanced ability to resist disease.

The objective of the present study was to further expand on that work using a population of 3715 Australian Angus steers and heifers with genotypes for 45 364 autosomal single-nucleotide polymorphisms (SNPs), and to provide the latest multivariate genomic estimates of heritability and genetic correlations for IDEX and the associated Cell-IR and Ab-IR immune competence phenotypes. In addition, accuracy, bias and dispersion of genomic predictions of breeding values (GEBV) for Cell-IR, Ab-IR and IDEX are presented and discussed.

Materials and methods

Animals and cohorts

In total, 2395 Angus steers and 1320 Angus heifers that were progeny from the Angus Sire Benchmarking Program (ASBP) were included in this study. Animals were from five year-of-birth (YOB) cohorts: 2012 (n = 497 animals from 48 sires), 2013 (n = 418 animals from 43 sires), 2016 (n = 1220 animals from 64 sires), 2017 (n = 925 animals from 56 sires) and 2018 (n = 655 animals from 43 sires), representing 12 herds and 232 sires from the ASBP. The ASBP is a major initiative of Angus Australia to generate progeny test data on modern Angus bulls, particularly for hard-to-measure traits such as feed efficiency, abattoir carcass measurements, meat-quality attributes, and female reproduction (https://www.angusaustralia.com.au/sire-benchmarking/about/general-information/).

By its own design, there exist minimal sire linkages across YOB cohorts in the ASBP. In our current dataset, there were three link sires between YOB cohorts 2012 and 2013, 14 link sires between YOB cohorts 2016 and 2017, two link sires between YOB cohorts 2016 and 2018, and five link sires between YOB cohorts 2017 and 2018.

Phenotypes and genotypes

On the basis of previously described protocols (Hine *et al.* 2019), the immune competence phenotype of animals was assessed using measures of both Cell-IR and Ab-IR. In brief, calves were vaccinated with Ultravac 7in1 clostridial and leptospira vaccine (Zoetis) on the day they were weaned. Calves were then given time to respond to the vaccination and Cell-IR was assessed by measuring the magnitude of delayed-type hypersensitivity reactions induced by intradermal injection of the clostridial and leptospira vaccine in the caudal fold of the tail. The Cell-IR trait is expressed for each animal as the increase in skin-fold thickness at the test site receiving the vaccine relative to the increase in skin-fold thickness observed at the control site receiving saline. To assess Ab-IR, the production of tetanus toxoid-specific IgG1 serum antibody was measured between Day 8 and Day 21 post-vaccination (depending on prior vaccination history), by using an enzyme-linked immunosorbent assay and results are reported in optical-density units. All animals within a herd-testing cohort had an identical vaccination history and were assessed for immune competence on the same day post-vaccination. To approximate normality, the immune competence phenotypes of Cell-IR and Ab-IR were log- and square root-transformed respectively. Finally, values were multiplied by 100 for numerical convenience.

Following Reverter *et al.* (2021), Cell-IR and Ab-IR were combined to generate IDEX as follows:

$$\text{IDEX} = [Z_{\text{CELL}} + (1 - |r|)Z_{\text{AB}}]\left(1 - \frac{|d\text{Rank}|}{n-1}\right).$$

where Z_{CELL} and Z_{AB} are the Z-score standardisation of Cell-IR and Ab-IR respectively; r is the Pearson correlation coefficient between Cell-IR and Ab-IR; and dRank is the difference in ranking of individuals for each metric.

In addition, genotypes for 45 364 autosomal SNPs were available for the 3715 animals included in the study, and were used to compute the genomic relationship matrix (G) following Method 1 of VanRaden (2008) with the modification of Karoui *et al.* (2012) to make it invertible, as follows:

$$\text{G} = 0.95 \cdot \frac{\text{SS}^T}{2\sum p_i(1-p_i)} + 0.05 \cdot \mathbf{I},$$

where **S** is the centred matrix relating SNP genotypes (recoded as 0, 1 or 2) in columns with animals in rows, and p_i is the frequency of the second allele of the ith SNP, and **I** is an identity matrix included to make Genomic Relationship Matrix invertible by enlarging the diagonal elements.

Genomic predictions and cross-validation models

Variance components, heritability (h^2), genetic (r_g) and residual (r_e) correlations were estimated on the basis of GBLUP methodology, by using the Qxpak5 software (Pérez-Enciso and Misztal 2011). For the genomic prediction models, we performed GBLUP analyses using a tri-variate (Cell-IR, Ab-IR and IDEX) mixed-effect model that contained the fixed effects of contemporary group (CG), and the linear covariates of age at measurement in days and the logarithm of the fold change in skin thickness at the control site. For each phenotype, CG contained animals of the same sex, YOB cohort, month of birth, property of origin, and date of measurement.

Additionally, the random additive polygenic and residual effects were fitted with assumed distributions N(**0**, **G**⊗**V**) and N(**0**, **I**⊗**R**) respectively, where **G** represents the genomic relationship matrix described earlier, **V** is the 3 × 3 genetic co-variance matrix, **I** is an identity matrix, **R** is the residual variance–covariance matrix and ⊗ represents the Kronecker product.

The tri-variate analysis was initially performed with the whole dataset of 3715 records. Then, for the cross-validation, the analysis was repeated five times, each after setting as missing values the records from animals of a given YOB cohort. The resulting GEBV from the analysis using the entire dataset are termed $\hat{u}_w$ to indicate that they are based on the *whole* dataset and will be used as the calibration. Similarly, the GEBV from the analyses that treated as missing values records from a given YOB cohort are termed $\hat{u}_p$ to indicate that they are based on *partial* data and will be used as the validation.

Traditional (Bolormaa *et al*. 2013) and Method LR (Legarra and Reverter 2018) approaches were used to estimate accuracy, bias and dispersion of GEBV. The following four metrics were employed:

(1) Traditional accuracy (ACC_T): in the context of cross-validation, the accuracy of a GEBV is traditionally computed from the Pearson correlation between a GEBV and the adjusted phenotype (y^*; phenotype y adjusted for fixed effects) for individuals in the validation population, and divided by the square root of heritability:

$$ACC_T = \frac{r(\hat{\boldsymbol{u}}_p, \boldsymbol{y}^*)}{\sqrt{h^2}}$$

(2) Method LR Accuracy (ACC_{LR}): for individuals in the validation population, Method LR accuracy was computed as follows:

$$ACC_{LR} = \sqrt{\frac{cov(\hat{\boldsymbol{u}}_w, \hat{\boldsymbol{u}}_p)}{(1 + \bar{F} - 2\bar{f})\sigma^2_{g,\infty}}}$$

where $\bar{F}$ is the average inbreeding coefficient, $2\bar{f}$ is the average relationship between individuals, and $\sigma^2_{g,\infty}$ is the genetic variance at equilibrium in a population under selection. Assuming the individuals in the validation population are not under selection, $\sigma^2_{g,\infty}$ can be approximated by the additive genetic variance estimated from the partial dataset.

(3) Method LR Bias ($Bias_{LR}$): difference between the average GEBV of individuals in the validation population using the partial data minus that using the whole data:

$$Bias_{LR} = \overline{\hat{\boldsymbol{u}}_p} - \overline{\hat{\boldsymbol{u}}_w}$$

In the absence of bias, the expected value of $Bias_{LR}$ is zero, whereas positive and negative values indicate respectively overestimation and underestimation of GEBV for validation animals when their own observation was not included.

(4) Method LR Dispersion ($Disp_{LR}$): for individuals in the validation population, dispersion was measured from the slope of the regression of $\hat{\boldsymbol{u}}_w$ on $\hat{\boldsymbol{u}}_p$:

$$Disp_{LR} = 1 - \frac{cov(\hat{\boldsymbol{u}}_w, \hat{\boldsymbol{u}}_p)}{var(\hat{\boldsymbol{u}}_p)}$$

In the absence of bias, the expected value of $Disp_{LR}$ is 0. Values less than 0 indicate under-dispersion (or deflation) of $\hat{\boldsymbol{u}}_p$ into $\hat{\boldsymbol{u}}_w$ as phenotypes become available. Values >1 indicate over-dispersion (or inflation) of $\hat{\boldsymbol{u}}_p$ into $\hat{\boldsymbol{u}}_w$.

Results and discussion

Phenotypes, genomic relationships and genetic parameters

Table 1 provides summary statistics for all phenotypes and covariates used in analyses. To approximate normality, the immune competence phenotypes for Cell-IR and Ab-IR were log- and square root-transformed respectively, and were consistent with the values reported by Reverter *et al*. (2021), using a subset of 2853 animals. Across all 3715 animals from the current study, and using raw unadjusted measurements, the correlation between Cell-IR and Ab-IR was moderately positive at 0.195 ± 0.016 and slightly higher for steers (0.206 ± 0.020) than for heifers (0.138 ± 0.027).

In agreement with theoretical expectations, the 3715 diagonal elements of the genomic relationship matrix **G** averaged 0.997, with a standard deviation (s.d.) of 0.028, and ranged from 0.912 to 1.131. Meanwhile, the 6 898 755 off-diagonal elements of **G** averaged –0.000, with a s.d. of 0.030 and ranged from –0.105 to 0.648. The similarity in the variance of diagonal and off-diagonal elements indicates both that a sufficiently large number of SNP was used to estimate relationships and the presence of a single-breed population (Simeone *et al*. 2011).

Genomic estimates of genetic variance (±standard error, s.e.) for Cell-IR, Ab-IR and IDEX were 17.093 (±2.852), 153.646 (±31.236) and 0.260 (±0.047) respectively.

Table 1. Summary statistics including mean, standard deviation (s.d.), minimum and maximum for the immune competence traits and covariates for the 3715 animals included in the study

Cell-IR, cell-mediated immune response (log-transformed); Ab-IR, antibody-mediated immune response (square-root transformed; OD, optical density); IDEX, ImmuneDEX; AGE, age at time of immune competence testing; CST, change in skin thickness at control site when assessing Cell-IR

Category/variable	Mean	s.d.	Min.	Max.
Immune competence trait				
Cell-IR (100 × log(mm))	26.939	9.497	–7.073	177.815
Ab-IR (100 × OD units)	86.535	24.817	14.021	145.954
IDEX	0.005	1.137	–4.457	9.127
Linear covariates				
AGE (days)	197.136	39.805	88.000	310.000
CST (log(mm))	–0.007	0.042	–0.194	0.252

Table 2 provide estimates of h^2, genetic and residual correlations across the three immune competence traits using the whole dataset. The estimates of h^2 for Cell-IR and Ab-IR were 0.247 ± 0.039 and 0.326 ± 0.059 respectively. These values are comparatively lower than the pedigree-based estimates recently reported by Reverter *et al*. (2021) of 0.31 ± 0.06 and 0.42 ± 0.06 respectively, for the same traits. The lower estimates can be attributed to several factors, including the use of genomic data here, the larger sample size and the analytical models (i.e. trivariate here vs the average of bivariate in the earlier work).

The estimated r_g between Cell-IR and Ab-IR was 0.138 ± 0.095, closer to zero and more precisely estimated because of the larger sample size than the 0.33 ± 0.12 (Reverter *et al*. 2021), 0.48 ± 0.19 (Hine *et al*. 2019) or the 0.40 ± 0.22 from Dominik *et al*. (2019) values reported previously. However, strongly positive estimates of genetic correlation were obtained between IDEX and Cell-IR (r_g = 0.740 ± 0.044) and between IDEX and Ab-IR (r_g = 0.741 ± 0.036). These high genetic correlation estimates between component traits and the composite trait are comparatively less extreme, but within two s.e., of the ones reported by Reverter *et al*. (2021) of 0.80 ± 0.05 (for IDEX and Cell-IR) and 0.85 ± 0.04 (for IDEX and Ab-IR). Taken together, these values anticipate the suitability of IDEX as a single phenotype to aid in the genetic improvement of immune competence and potentially general disease resistance in the current population.

Further research is needed to (re)evaluate the relationship between the immune competence phenotypes analysed here and productivity-based phenotypes related to growth, feedlot performance and carcass characteristics. In particular, it would be of interest to recapitulate the negative genetic correlation between the immune competence traits and the growth traits, such as –0.38 ± 0.14 between IDEX and the weaning weight estimated by Reverter *et al*. (2021). Such finding would agree with previous reports showing that selection for productivity, with no emphasis on health and fitness traits, has increased susceptibility to disease in many species of food-producing animals (Rauw *et al*. 1998).

Table 2. Estimates (±s.e.) for heritability (bold, diagonal), genetic (above diagonal) and residual (below diagonal) correlations for the three immune competence traits: cell-mediated immune response (Cell-IR, log-transformed), antibody-mediated immune response (Ab-IR; square-root transformed) and ImmuneDEX (IDEX)

Trait	Cell-IR	Ab-IR	IDEX
Cell-IR	**0.247 ± 0.039**	0.138 ± 0.095	0.740 ± 0.044
Ab-IR	0.115 ± 0.047	**0.326 ± 0.059**	0.741 ± 0.036
IDEX	0.755 ± 0.019	0.677 ± 0.032	**0.275 ± 0.045**

Accuracy, bias and dispersion of GEBV

Table 3 shows the ACC_T and ACC_{LR} of GEBVs for the three immune competence traits when each consecutive YOB cohort was used as the validation population. While there was a strong correlation between ACC_T and ACC_{LR} across the 15 measures (r = 0.831 ± 0.154), on average, the ACC_{LR} accuracies were 38% higher than the ACC_T accuracies (0.420 vs 0.304). Averaged across the five YOB cohorts, the highest accuracy was observed for Ab-IR (ACC_T=0.348, ACC_{LR} = 0.443), which could be attributed to its higher h^2 estimate (0.326 ± 0.059; Table 2). With a reference population of 4000 animals,

Table 3. Traditional (ACC_T) and method LR (ACC_{LR}) accuracies of GEBVs for the three immune competence traits, namely, cell-mediated immune response (Cell-IR, log-transformed), antibody-mediated immune response (Ab-IR; square-root transformed) and ImmuneDEX (IDEX), when each consecutive YOB cohort was used as the validation population

Trait	YOB cohort (number of animals)					Mean
	2012 (n = 497)	2013 (n = 418)	2016 (n = 1220)	2017 (n = 925)	2018 (n = 655)	
			ACC_T			
Cell-IR	0.310	0.263	0.255	0.361	0.249	0.288
Ab-IR	0.355	0.327	0.365	0.393	0.299	0.348
IDEX	0.263	0.203	0.269	0.371	0.269	0.275
			ACC_{LR}			
Cell-IR	0.382	0.395	0.386	0.435	0.426	0.405
Ab-IR	0.449	0.419	0.450	0.480	0.420	0.443
IDEX	0.399	0.389	0.396	0.466	0.408	0.411

Table 4. Bias and dispersion (±s.e.) of GEBVs for the three immune competence traits, namely, cell-mediated immune response (Cell-IR, log-transformed), antibody-mediated immune response (Ab-IR; square-root transformed) and ImmuneDEX (IDEX), when each YOB cohort was used as the validation population

Trait	YOB cohort (number of animals)				
	2012 (n = 497)	2013 (n = 418)	2016 (n = 1220)	2017 (n = 925)	2018 (n = 655)
			Bias		
Cell-IR	–0.109 ± 0.098	0.130 ± 0.080	0.008 ± 0.065	0.034 ± 0.062	–0.048 ± 0.081
Ab-IR	–0.157 ± 0.299	–0.283 ± 0.269	–0.155 ± 0.201	–0.193 ± 0.230	–0.133 ± 0.250
IDEX	–0.016 ± 0.013	0.002 ± 0.010	–0.004 ± 0.009	–0.004 ± 0.009	–0.008 ± 0.010
			Dispersion		
Cell-IR	0.019 ± 0.063	0.146 ± 0.043	0.190 ± 0.034	0.050 ± 0.032	0.137 ± 0.041
Ab-IR	0.026 ± 0.053	0.142 ± 0.046	–0.026 ± 0.037	0.027 ± 0.040	0.196 ± 0.042
IDEX	0.050 ± 0.063	0.210 ± 0.044	0.147 ± 0.039	0.041 ± 0.035	0.171 ± 0.041

a h^2 of 0.3 and an effective population size (N_e) of 100, the expected GEBV accuracy is ~0.45 (fig. 3*b* in Goddard and Hayes 2009). Similarly, with a reference population of 1743 Australian Angus cattle, Bolormaa *et al*. (2013) reported a GEBV accuracy of 0.26 averaged across 16 traits. De Roos *et al*. (2008) estimated N_e in Australian Holstein–Friesian, Jersey and Angus cattle and found that the N_e for these breeds has decreased over the past 50 generations, to ~100. Therefore, averaged across the three traits, the ACC_{LR} at 0.420 (compared with ACC_T at 0.304) is closer to the theoretical expectation.

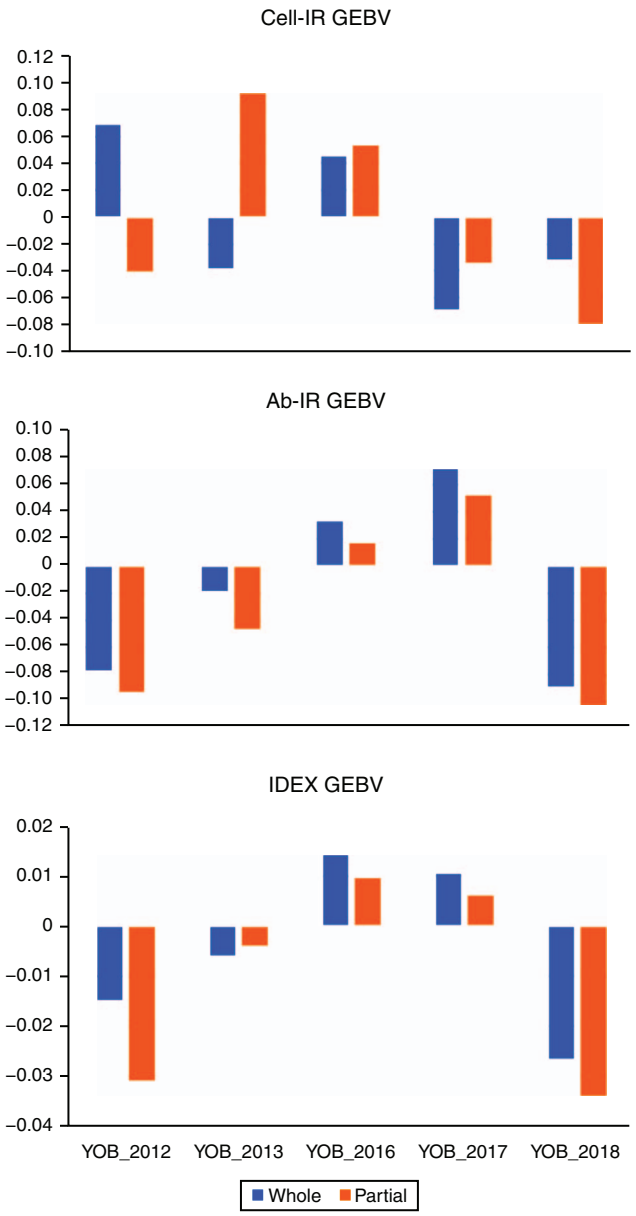

Fig. 1. Average GEBV by each YOB cohort for the three immune competence traits, Cell-IR (top panel), Ab-IR (middle panel) and IDEX (bottom panel) estimated using either the whole data (blue bars) or partial data (orange bars) where the phenotypes of the YOB cohort were treated as missing values.

It is worth noting that the complete dataset was used to obtain estimates of CG fixed effects and covariates, and these estimates were used to adjust the phenotypes of individuals in the validation population, and with adjusted phenotypes needed in the computation of ACC_T. Animals in validation and training sets were raised in different CGs. Therefore, the only linkage between them is through genomic relationships and no link was created as a consequence of using records in the validation sets to obtain the estimates to accomplish the precorrection.

Table 4 lists the estimates of GEBV bias and dispersion for the three IC traits when using each consecutive YOB cohort as the validation population. In 4 of the 15 instances (3 traits × 5 YOB cohorts), zero was not contained in the interval spanned by bias ± 1 s.e. Two of these four instances corresponded to Cell-IR using the 2012 and 2013 YOB cohorts with negative and positive bias respectively. This could be attributed to 2012 and 2013, being the smallest YOB cohorts and, hence, more prone to sampling variation. To aid in the interpretation of estimates of bias presented in Table 4, Fig. 1 shows the average GEBV by each YOB cohort for the three immune competence traits, Cell-IR (top panel), Ab-IR (middle panel) and IDEX (bottom panel), estimated using either the whole data (blue bars and termed $\hat{u}_w$) or partial data (orange bars and termed $\hat{u}_p$) where the phenotypes of the YOB cohort were treated as missing values. Only for Cell-IR and YOB cohort 2012 and 2013 were the GEBV on the basis of whole or partial data in opposite sign, on average.

Similarly, the estimates of GEBV dispersion for Cell-IR and IDEX show that in four of the five YOB cohorts, the interval spanned by dispersion ± 1 s.e. was on the positive side, indicating overdispersion. This overdispersion can be attributed to higher h^2 estimates when phenotypes of the YOB cohort were treated as missing values compared with h^2 estimates using the whole dataset (Fig. 2).

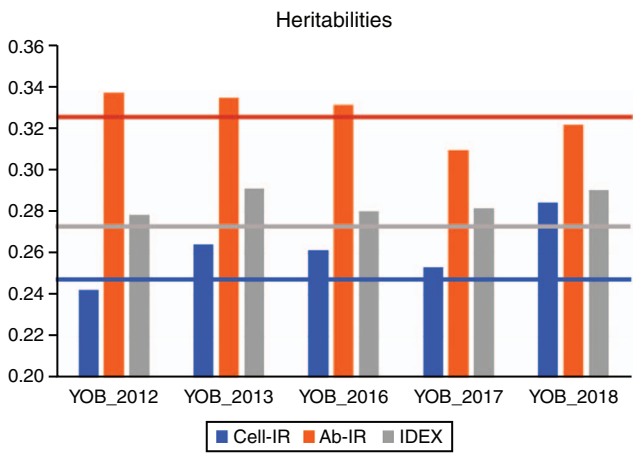

Fig. 2. Heritability estimates for the three immune competence traits, Cell-IR (blue bars), Ab-IR (orange bars) and IDEX (grey bars), by each YOB cohort where the phenotypes of the YOB cohort were treated as missing values. Horizontal bars correspond to estimates obtained using the whole dataset (Table 2).

Conclusions

In conclusion, the current study expands on our recently published study introducing ImmuneDEX (Reverter *et al.* 2021) in four major aspects, as follows: (1) that earlier work focused on the analytical methodology to combine both metrics of immune competence, cell- and antibody-meditated immune response into a single metric, namely ImmuneDEX; (2) the sample size has increased by 30% (or from 2853 before to 3715 now); (3) we now use genomic information to estimate genetic parameters; and (4) we place emphasis on the quality of the resulting GEBVs on the basis of their accuracy, bias and dispersion and using YOB cohorts in a cross-validation scheme to generate the testing populations that, while all comprising Australian Angus cattle, are very poorly related among themselves.

Taken together, and consistent with previous findings, immune competence phenotypes are moderately heritable and accurate GEBVs can be generated for immune competence to allow for selection of cattle with an improved ability to mount an immune response. Our analyses suggest that ImmuneDEX will provide a tool to underpin long-term genetic strategies aimed at improving the immune competence of animals in production systems, which in turn is expected to reduce the incidence of disease and our reliance on antibiotics to treat disease.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

This work was co-funded by Meat and Livestock Australia (MLA) (MLA, on behalf of the Australian Lot Feeders' Association), Angus Australia and CSIRO. The authors acknowledge Angus Australia for facilitating access to progeny from the Angus Sire Benchmarking Program for testing and associated data. We gratefully acknowledge cooperating herd owners, managers, and staff. Special thanks go to Sue Belson, Jim Lea, and Grant Uphill for their technical assistance.

References

Bolormaa S, Pryce JE, Kemper K, Savin K, Hayes BJ, Barendse W, Zhang Y, Reich CM, Mason BA, Bunch RJ, Harrison BE, Reverter A, Herd RM, Tier B, Graser H-U, Goddard ME (2013) Accuracy of prediction of genomic breeding values for residual feed intake, carcass and meat quality traits in *Bos taurus*, *Bos indicus* and composite beef cattle. *Journal of Animal Science* **91**, 3088–3104. doi:10.2527/jas.2012-5827

de Roos AP, Hayes BJ, Spelman RJ, Goddard ME (2008) Linkage disequilibrium and persistence of phase in Holstein–Friesian, Jersey and Angus cattle. *Genetics* **179**, 1503–1512. doi:10.1534/genetics.107.084301

Dominik S, Porto-Neto LR, Duff CJ, Byrne AI, Hine BC, Ingham A, Colditz IG, Reverter A (2019) A method for developing a breeding objective trait from multiple components using the example of immune competence in Australian Angus cattle. *Proceedings of the Association for the Advancement of Animal Breeding and Genetics* **23**, 402–405.

Goddard M, Hayes B (2009) Mapping genes for complex traits in domestic animals and their use in breeding programmes. *Nature Reviews Genetics* **10**, 381–391. doi:10.1038/nrg2575

Hine BC, Bell AM, Niemeyer DOD, Duff CJ, Butcher NM, Dominik S, Ingham AB, Colditz I (2019) Immune competence traits assessed during the stress of weaning are heritable and favourably genetically correlated with temperament traits in Angus cattle. *Journal of Animal Science* **97**, 4053–4065. doi:10.1093/jas/skz260

Karoui S, Carabano MJ, Diaz C, Legarra A (2012) Joint genomic evaluation of French dairy cattle breeds using multiple-trait models. *Genetics, Selection, Evolution* **44**, 39. doi:10.1186/1297-9686-44-39

Legarra A, Reverter A (2018) Semi-parametric estimates of population accuracy and bias of predictions of breeding values and future phenotypes using the LR method. *Genetics, Selection, Evolution* **50**, 53. doi:10.1186/s12711-018-0426-6

Pérez-Enciso M, Misztal I (2011) Qxpak.5: old mixed model solutions for new genomics problems. *BMC Bioinformatics* **12**, 202. doi:10.1186/1471-2105-12-202

Rauw WM, Kanis E, Noordhuizen-Stassen EN, Grommers FJ (1998) Undesirable side effects of selection for high production efficiency in farm animals: a review. *Livestock Production Science* **56**, 15–33. doi:10.1016/S0301-6226(98)00147-X

Reverter A, Hine BC, Porto-Neto L, Li Y, Duff CJ, Dominik S, Ingham AB (2021) ImmuneDEX: a strategy for the genetic improvement of immune competence in Australian Angus cattle. *Journal of Animal Science* **99**, skaa384. doi:10.1093/jas/skaa384

Simeone R, Misztal I, Aguilar I, Legarra A (2011) Evaluation of the utility of diagonal elements of the genomic relationship matrix as a diagnostic tool to detect mislabelled genotyped animals in a broiler chicken population. *Journal of Animal Breeding and Genetics* **128**, 386–393. doi:10.1111/j.1439-0388.2011.00926.x

VanRaden PM (2008) Efficient methods to compute genomic predictions. *Journal of Dairy Science* **91**, 4414–4423. doi:10.3168/jds.2007-0980

Wilkie B, Mallard B (1999) Selection for high immune response: an alternative approach to animal health maintenance? *Veterinary Immunology and Immunopathology* **72**, 231–235. doi:10.1016/S0165-2427(99)00136-1

Handling editor: Sue Hatcher