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Evaluation of Zoetis GeneMax Advantage genomic predictions in commercial *Bos taurus* Angus cattle¹

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ABSTRACT: The GeneMax (GMX) Advantage test, developed by Zoetis, uses approximately 50,000 single nucleotide polymorphisms (SNP) to predict the genomic potential of a commercial Angus heifer. Genetic predictions are provided for Calving Ease Maternal, Weaning Weight, Heifer Pregnancy, Milk, Mature Weight, Dry Matter Intake, Carcass Weight, Marbling, and Yield. Indices of economically important traits are estimated on an index score (1-100 scale) and are divided into three indices; Cow Advantage index, Feeder Advantage index, and Total Advantage index. The indices provide a genomic prediction of the profitability of the cow's calves. Therefore, test results can inform selection and culling decisions made by commercial beef cattle producers. To measure the accuracy of the trait predictions, data from commercial Angus females and their progeny at the University of Missouri Thompson Research Center was utilized to analyze weaning weight, milk, marbling, fat, ribeye area, and carcass weight. Progeny phenotypic data was matched to the respective dam, then the cow's genomic predictions were compared to the calf's age-adjusted phenotypes using correlation and linear models. All tested GeneMax scores of the dam were significantly correlated with and predicted calf performance. Our predicted effect sizes, except for fat thickness, were similar to those reported by Zoetis. In conclusion, the GeneMax Advantage test accurately ranks animals based on their genetic merit and is an effective selection tool in commercial cowherds.

Key words: genomic prediction, validation, *Bos taurus*, growth, carcass

INTRODUCTION

Prediction of quantitative traits using DNA markers in beef cattle was first commercialized in the 1990s. However, many of these tests relied on a small number of markers and failed validation trials (Van Eenennaam et al., 2007). Genomic prediction, the use of thousands of genome-wide DNA markers (Nejati-Javaremi et al., 1997; Meuwissen et al., 2001), has proven to be a much more efficacious strategy in driving genetic improvement (García-Ruiz et al., 2016; Taylor et al., 2016). Still, many farmers, ranchers (Weaber et al., 2014), extension professionals, and even academics question the effectiveness of genomic prediction in commercial beef cattle. Demonstrations of the ability of genomic tests to accurately predict genetic merit may encourage farmers and ranchers to adopt this technology and accelerate genetic progress in commercial herds. Our objective is to evaluate the effectiveness of the Zoetis GeneMax Advantage (genomic predictions designed for commercial heifers) in predicting the genetic merit of Angus cattle. We hypothesize that, because this test was built using principles of genomic prediction, the dam's GeneMax scores will significantly predict her calves' performance.

MATERIALS AND METHODS

An Animal Care and Use Committee protocol is not necessary for this project as DNA samples were collected as part of routine animal production practices. However, the University of Missouri has a demonstration ACUC protocol, number 7491, which covers the procedures used in this research. Phenotypic and pedigree data were collected at the University of Missouri's Thompson Research Center and entered into Angus Genetics Inc. Beef Improvement Records (BIR) program through

AngusOnline.org. Pedigree, phenotype, and GeneMax Advantage score information were retrieved as Excel files from AngusOnline.org in June of 2018. Phenotypic records were collected from 1995 to 2018, however only calves born from 2003 to 2011 and from 2014 to 2018 had data reported to BIR and genotyped dams (**Figure 1**). Summary statistics are presented in **Table 1**. Excel files were read into R (Team, 2018) and similar files from different years were combined. Packages utilized included readr (Wickham et al., 2018b), ggplot2 (Wickham, 2016), tidyr (Wickham and Henry, 2018), dplyr (Wickham et al., 2018a), and stringr (Wickham, 2018).

For statistical analyses, the calf phenotype was compared with the dam's GeneMax score. For each of the traits, Pearson and Spearman correlations were calculated.

To control for potential confounding factors, mixed models were used to evaluate the relationship between calf phenotype and dam's GeneMax Score. We used the model:

$$y = X\beta + Zu + e$$

where, y is the phenotype of the calf; β are fixed effects of year of birth, sex, and dam GMX Score; u is the random effect of sire, and e is the residual. Both u and e are $\sim N(0, I)$. There were 47 bulls who sired calves with weaning weight records, 37 bulls who sired calves with hot carcass weight, marbling, and ribeye area records, and 23 bulls who sired calves with fat thickness records. For each of the traits, three models were compared: a full model including dam GMX Score and the random effect of sire, a reduced model that did not include the effect of sire, and a reduced model that did not include the effect of dam GMX Score. For growth traits, the birth year of the calf was considered the contemporary group. For carcass traits, contemporary group was defined by the harvest date. For each trait, a χ^2 test was run between

the first and second models to determine if the inclusion of the random effect of sire was significant. A χ^2 test was also run between the first and third models to determine the significance of the inclusion of the cow's GeneMax Advantage score. For weaning weight, we also fit models that included age-of-dam as a fixed effect factor and dam as a random effect. Further, a model was also executed that included both Weaning Weight (WW) GMX Score and Milk GMX Score. Models containing 1) WW GMX Score, 2) Milk GMX Score, and 3) WW and Milk GMX Scores were compared to see which best fit the data. Because there is a trend over time for weaning weight phenotypes and we do not have a random sample of DNA tested cows, calves born in the early 2000s may have low weaning weights compared to calves born in later years (**Figure 1d**) but ranked high in their own contemporary group (weaning weight ratio, **Figure 1e**). Thus, we also measured the association between the dam's GMX WW scores and GMX Milk scores with the calf's weaning weight ratio (no contemporary group effect was included in these models).

Estimates of GeneMax Advantage score effects were retrieved from Zoetis technical bulletin GMX-00116 (Zoetis Genetics and Angus Genetics Inc., 2018). Effects were converted from Imperial to scientific units, divided by 10 to represent a 1-point GeneMax score increase, and divided by 2 to change from molecular breeding values to expected progeny differences (transmitting abilities). Our GeneMax score effect estimates were compared to Zoetis' published estimates using a two-tailed Z-test.

Results

For each trait evaluated, the Pearson's correlation and Spearman's correlation between the calf's phenotype and the dam's GMX Score were statistically different from zero (**Table 2**). Further, from the six regression models, the dam's GMX Score had a significant effect on the calf's phenotype (**Table 3**). Except for fat thickness, our estimated effect sizes were not statistically different compared with those published by Zoetis (**Table 3**). When weaning weight was adjusted for age-of-dam as a factor and a random effect of dam, the estimated effect of a 1-point change in WW GMX Score increased to 0.29 ± 0.08 kg (p-value = $6.4e-4$). Conversely, when Milk GMX Score was evaluated in a model containing age-of-dam, random dam effect, or both, the estimated effect of Milk GMX Score was not different from zero (p-value > 0.9). When weaning weight ratio was the dependent variable to more accurately account for an animal's rank in its contemporary group, WW GMX score was significantly predictive in the simple model with sex and random sire (0.08944 ± 0.02057 , p-value = $1.8e-05$) and in the more complicated model with age-of-dam and random dam effect (0.1011 ± 0.0321 , p-value = 0.002). When Milk GMX Score was compared to weaning weight ratio, the effect was not significant (p-value = 0.16). A model containing both GMX WW Score and GMX Milk Score provided a better fit to the data and estimated larger effects for the GMX Scores compared with the models using one GMX Score (**Table 4**). Calf phenotypes were plotted against dam's GMX Score in **Figure 2**.

Discussion

In the last ten years, the use of DNA information to produce genomic predictions has changed substantially. For example, when first launched in 2010, the IGENITY MBVs (molecular breeding values) were only based on 384 DNA markers (Weber et al., 2012). However, even the initial genomic predictions (which were used as indicator traits in a multi-step genomic-enhanced

EPD analysis) trained with a couple thousand animals accurately predicted genetic merit (Weber et al., 2012). In the last ten years, hundreds of thousands of beef cattle have been genotyped from multiple breeds, increasing the power of these datasets not just for genetic prediction, but also for basic research (Decker, 2015). Since 2015, breed associations have switched to single-step methods, in which pedigree and genomic data are combined in a single analysis (Lourenco et al., 2015). Pedigree information is not typically known for commercial cattle, so a DNA marker effects model is typically used to predict genetic merit for commercial cattle. However, the estimated breeding values produced by a genomic relationship model and a marker effects model are equivalent (Hayes et al., 2009). The marker effects used to calculate GMX scores in the Zoetis GeneMax Advantage test are based off of the American Angus Association single-step BLUP analysis (Zoetis Genetics and Angus Genetics Inc., 2018).

All traits had relatively weak correlations between the calf's phenotype and the dam's GMX Score. However, this is to be expected as this analysis does not account for Mendelian sampling (random shuffle of genes between generations), contemporary group effects (management and environment effects), sire effects, or the heritability of the trait. Nevertheless, as all correlations were significantly different from zero, it does demonstrate the predictive ability of the GeneMax Advantage test.

Regression analysis allowed a more sophisticated evaluation of the relationship between a dam's GMX Score and her calf's phenotype. These models accounted for variation due to sex, year of birth or slaughter date, and sire effects. However, this model still did not account for Mendelian sampling or other non-additive genetic effects, including genotype-by-environment effects. The

amount of variation due to Mendelian sampling is large and theoretically equal to half of the additive genetic variance. These sources of variation are likely why we still observe substantial spread around the regression lines in **Figure 2**. Genetic predictions are not designed to predict performance of individual animals, but rather the average performance of a large group of progeny out of a parent compared to the progeny average of a different parent or population average. Our results show that the GeneMax Advantage test accurately predicts the average progeny performance for weaning weight, milk, marbling, carcass weight, ribeye area and fat thickness. Our estimates of the effects of GeneMax scores, except for fat thickness, in a validation population were not significantly different from those published by Zoetis.

Regardless of whether we expressed weaning growth as a weight or as a ratio within contemporary group, WW GMX Score accurately predicted variation in weaning growth. Further, when we adjusted for age-of-dam and accounted for dependency between data with a random dam effect, the magnitude the WW GMX effect increased from 0.18 to 0.29. This larger estimate is closer to that published by Zoetis. However, Milk GMX scores were not predictive of weaning weight ratio or when more complicated models were used. This likely reflects the well-known difficulty of predicting maternal effects (Willham, 1980). For example, in the 2014 Angus genomic-enhanced EPD calibration based on 57,550 animals, the correlation between weaning weight and Milk EPD was 0.36. The average of the other traits was 0.66 (range of 0.45 to 0.78). In 2016, when 108,211 animals were used to estimate molecular breeding values, the correlation between weaning weight and Milk EPD was 0.37, range of 0.56 to 0.80 for other traits (Albers, 2016). Further, only 491 observations were available when analyzing weaning weight ratio or age-of-dam effects, compared to 781 observations for the models that only fit

contemporary group, sex, and sire. Thus, the difficulty of predicting maternal effects and the smaller sample sizes affected the more complicated Milk GMX models.

We note that the Zoetis GeneMax Advantage prediction is designed to work in high-percentage Angus animals and is not designed for cattle with substantial ancestry from other breeds (Kachman et al., 2013). However, other similar genomic predictions for crossbred cattle should be equally accurate provided they contain the appropriate breeds in a large, multi-breed training population.

Genetic predictions, whether based on pedigree or genomic relationships, work when trained using ample and appropriately structured data. Models using contemporary group effects and random effects to account for covariance between relatives appropriately separate additive genetic variation from other sources of variation, including management and environment. While genetic predictions were never intended to predict the performance of a single individual, the average progeny performance is accurately predicted by the additive genetic merit of the parent. However, biological variation remains, including non-additive genetic effects and interactions (Smith et al., 2019; Braz et al., 2020) and especially Mendelian sampling (Cole and VanRaden, 2011) between full- or half-siblings. The increased adoption of genomic technologies in commercial cattle production has the opportunity to significantly increase long-term genetic gain through more accurate replacement animal selection.

Conclusions

Genomic predictions, including the Zoetis GeneMax Advantage, accurately predict a straightbred, commercial Angus animal's genetic merit and the average performance of their offspring. Academics and extension professionals can confidently state to farmers and ranchers that genomic predictions in commercial animals are accurate and effective.

Disclosures

The authors declare no competing interests.

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287 *Tables and Figures*

288 **Table 1.** Summary statistics of data used for GeneMax Advantage evaluation.

	Number (Number with matched calves)	Mean	Standard Deviation	Median	Minimum	Maximum	Range	Skew	Kurtosis
Weaning Weight, kg	781	263.01	26.3	264.44	178.26	347.45	169.19	-0.17	3.05
Weaning Weight Ratio	491	100.05	9.04	100	67	130	63	-0.08	3.53
Marbling Score	374	6.53	1.14	6.55	3.2	9.2	6	-0.22	3.1
Hot Carcass Weight, kg	376	398.65	40.31	401.88	249.48	504.85	255.37	-0.62	3.93
Fat Thickness, cm	290	1.77	0.48	1.7	0.53	4.14	3.61	1.1	6.33
Ribeye Area, cm²	374	84.79	9.31	84.52	57.42	112.9	55.48	0.12	2.87
WW GMX Score	554 (231)	45.59	20.39	45	3	97	94	0.19	2.27
Milk GMX Score	554 (231)	51.57	21.17	53	3	97	94	-0.14	2.18
CW GMX Score	554 (196)	49.18	19.41	48	7	95	88	0.11	2.27
Marb GMX Score	555 (196)	64.33	21.2	67	7	98	91	-0.44	2.25
RE GMX Score	556 (196)	50.54	20.07	49	7	97	90	0.19	2.06

Fat GMX Score	557 (188)	43.28	19.85	42	3	93	90	0.26	2.18
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Table 2. Pearson and Spearman correlation tests between the dam's Zoetis GeneMax Advantage Score (Kalamazoo, MI) and the calf's phenotype.

GeneMax Trait	Pearson Correlation (95% Confidence Interval)	Pearson Correlation P-value	Spearman Correlation	Spearman Correlation P-value
Weaning Weight	0.178 (0.109 to 0.245)	5.4e-07	0.182	3.0e-07
Maternal Milk	0.183 (0.114 to 0.250)	2.5e-07	0.162	5.3e-06
Marbling	0.273 (0.176 to 0.364)	8.4e-08	0.247	1.3e-06
Carcass Weight	0.125 (0.024 to 0.223)	1.5e-02	0.145	4.8e-03
Fat Thickness	-0.181 (-0.291 to -0.068)	1.9e-03	-0.191	1.1e-03
Ribeye Area	0.120 (0.019 to 0.219)	2.0e-02	0.112	3.0e-02

Table 3. Estimated effects of GMX Scores on production traits. Each row represents a different linear mixed model. Models contained contemporary group and sex as fixed effects and sire as a random effect. Difference from zero P -values from χ^2 test comparing full and reduced model. Difference from Zoetis effects estimated from a Z-test.

GMX Score	Estimate	Std. Error	t-value	Difference from zero P-value	Zoetis effect	Difference from Zoetis P-value
WW	0.18 kg	0.04 kg	4.43	1.1e-05	0.25 kg	0.08
Milk	0.13 kg	0.04 kg	3.62	3.2e-04	0.14 kg	0.88
Marb	0.01	0.002	4.97	1.1e-06	0.01	0.21
CW	0.20 kg	0.09 kg	2.14	3.3e-02	0.32 kg	0.19
RE	0.06 cm ²	0.02 cm ²	3.10	2.2e-03	0.07 cm ²	0.58
Fat	-0.003 cm	0.001 cm	-2.34	2.0e-02	-0.03 cm	<1.0e-22

299 **Table 4.** Estimated effects of dam's WW and Milk GMX Scores on calf's weaning weight. *P*-
 300 values from χ^2 test comparing full model with both traits versus reduced models with single trait.

GMX Score	Estimate	Std. Error	t-value	<i>P</i>-value
WW	0.20 kg	0.04 kg	4.92	1.0e-06
Milk	0.15 kg	0.04 kg	4.20	3.0e-05

Figure 1. Graphical summary of data available for analysis. a) Counts of animals by sex. An animal can be counted as both a bull and a steer, for example if it was a bull at weaning but castrated prior to entering the feedlot. b) Counts of animals by birth month and year. c) Counts of animals by slaughter month and year. d) Weaning weight plotted against birth date. e) Weaning weight ratio plotted against birth date.

Figure 2. Calf's phenotype plotted against dam's GMX Score. a) Weaning weight versus WW GMX Score, b) Weaning weight versus Milk GMX Score, c) Carcass weight versus CW GMX Score, d) Marbling score versus Marb GMX Score, e) Ribeye area versus RE GMX Score, and f) Fat Thickness versus Fat GMX Score. Red line represents the intercept and slope estimated from the linear models reported in Table 3.