

Delivering genomics to the beef herd

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Outline

How can DNA help accelerate genetic progress? Why genomics helps the dairy industry Why genomics is harder in the beef industry Current products on the market for beef Status of incorporation of DNA information into U.S. national beef cattle evaluations How can I use DNA-information to make money? Implications of genomics to industry structure



Animal breeders have used the resemblance between relatives to select parents of the next generation and make genetic change







Rate of genetic change (ΔG) is accelerated when breeders can accurately identify those individuals that have the best genetics at a young age

 $\Delta G =$

intensity of selection X



(v/genetic variance in population



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What is a Genetic Marker ?

A DNA sequence variation that has been associated with a given trait in one or more populations





Animal Genomics and Biotechnology Education

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We want to use DNA markers (SNPs) in addition to pedigree and performance information to help select the best animals







Information sources for EPDs – DNA just one source of data for GE-EPD



Genomic-Enhanced EPDs (GE-EPD)

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High-throughput genotyping technology enabled the development of high density "SNP chips"

The sequencing of the bovine genome allowed for the development of a 50,000 SNP chip, then the 800,000 SNP chip; and now whole genome sequence (3 billion)!





We can use these SNP CHIPS for "genomic" selection?

TRAINING POPULATION

1,000s animals

- Phenotypes
- Genotypes

Training = estimate the value of every chromosome fragment contributing variation in a population with phenotypic observations

Prediction = the results of training can then be used to develop prediction equations to predict the merit of new animals (e.g. young bulls)



Dairy industry ideally suited to increasing rate of genetic gain (AG) using genomic selection

- Mostly one breed
- High use of AI
- Clear selection goal (\$ net merit)



- Large number of high accuracy A.I. sires for training
- Extensive, uniform collection of data on traits
- Central evaluation (AIPL) receiving genotypes
- Obvious way to decrease age of selection in sires
- Al companies funding the genotyping because they get a clear cost savings in terms of young sire program



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> 400,000 Genotypes run in US dairy cattle









The Beef Cattle Industry

- Little use of AI
- Relatively few high accuracy sires for training
- Multiple competing selection goals cow/calf, feedlot, processor – little data sharing between sectors
- Few/no records on many economically-relevant traits
- Many breeds, some small with limited resources
- Crossbreeding is important
- No centralized "national" cattle evaluation
- Not clear who should pay for testing breeders? Breed associations? public funds ?



Translational Questions for the Beef Industry

- ? How many phenotypic records and animals are required in the training population?
- ? How does the relationship between the training population and the selection candidate affect accuracy of prediction?
- Popredictions work across breeds? Or only within breed
- ? How many markers are needed— 1, 384, 50K, 800K, genome?
- ? How often do prediction have to be recalibrated especially hard to measure traits as measurement is hard/expensive?
- ? What is the value generated by these tests do they pay?
- ? Does this technology change optimal breeding program design?



CALIFORNIA

Technology developers had a rocky start in the beef industry



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384 SNP chip assay

The Power of the IGENITY[®] profile for Angus

The American Angus Association® through its subsidiary, Angus Genetics Inc.® (AGI), has a vision to provide Angus breeders with the most advanced solutions to their genetic selection and management needs.

- 1. Dry Matter Intake
- 2. Birth Weight
- 3. Mature Height
- 4. Mature Weight
- 5. Milk
- 6. Scrotal Circumference
- 7. Weaning Weight
- 8. Yearling Weight
- 9. Marbling
- 10. Ribeye Area
- **11. Fat Thickness**
- 12. Carcass Weight
- 13. Tenderness
- 14. Percent Choice (quality grade)
- **15. Heifer Pregnancy**
- **16. Maternal Calving Ease**
- **17. Direct Calving Ease**
- **18. Docility**
- 19. Average Daily Gain
- **20. Feed Efficiency**
- 21. Yearling Height

Arthrogryposis Multiplex (AM)

Neuropathic Hydrocephalus (NH)

Bovine Viral Diarrhea – Persistently Infected (BVD Pi)

Coat Color



- 1. Calving ease direct
- 2. Birth weight
- 3. Weaning weight
- 4. Yearling weight
- 5. Yearling height
- 6. Mature weight
- 7. Mature height
- 8. Dry matter intake
- 9. Residual feed intake
- 10. Scrotal circumference
- 11. Docility
- 12.- Calving ease maternal
- 13. Milking ability
- 14. Carcass weight
- 15. Fat thickness
- 16. Ribeye area
- 17.- Marbling score
- 18. Tenderness







Pfizer Animal Health Animal Genetics 50K SNP chip assays 50,000 SNPs spread throughout genome





G A R Prede	stine	ed													13395344
	CED	BW	WW	YW	ADG	DMI	NFI	CEM	MA	CW	FAT	REA	MS	TND	\$B/\$MVP⁼-
EPD	7	4.1	53	99	-	-	-	6	28	26	0.046	0.59	1.07	-	69.78
ACC	0.84	0.97	0.96	0.94	-	-	-	0.8	0.85	0.82	0.81	0.82	0.84	-	-
EPD % Rank	30	85	15	15	-	-	-	55	10	4	90	2	1	-	1
MVP	13	1.0	37	-	0.45	0.97	0.04	8	33	55	0.07	0.92	1.52	-0.43	243
MVP % Rank	3	70	10	-	30	90	90	4	1	1	90	1	1	80	1



Need to integrate DNA information into National Cattle Evaluation (NCE)

"Information from DNA tests only has value in selection when incorporated with all other available forms of performance information for economically important traits in National Cattle Evaluation (NCE), and when communicated in the form of an EPD with a corresponding BIF accuracy.

For some economically important traits (e.g. feed efficiency), information other than DNA tests may not be available. Selection tools based on these tests should still be expressed as EPD within the normal parameters of NCE" (Tess, 2008).



Genomic-Enhanced EPDs (GE-EPD)



Realized accuracies (r) resulting from genomic selection prediction equations trained in US beef cattle breeds

Trait	Red Angus (6,412) ^b	Angus (3,500)	Hereford (2,980)	Simmental (2,800)	Limousin (2,400)	Gelbvieh (1,181)
Birth weight	0.75	0.64	0.68	0.65	0.58	0.41
Wean weight	0.67	0.67	0.52	0.52	0.58	0.34
Yearling weight	0.69	0.75	0.60	0.45	0.76	_
Milk	0.51	0.51	0.37	0.34	0.46	0.34
Fat thickness	0.90	0.70	0.48	0.29	—	—
Rib eye area	0.75	0.75	0.49	0.59	0.63	0.48
Marbling	0.85	0.80	0.43	0.63	0.65	0.56
Calving ease direct	0.60	0.69	0.68	0.45	0.52	0.48
Calving ease (maternal)	0.32	0.73	0.51	0.32	0.51	_
Scrotal circumference	—	0.71	0.43	—	0.45	0.50

^aData taken from References 29, 30, 131; D. Garrick, unpublished data (personal communication).

^bNumbers indicate training population. The Red Angus training data set includes some Black Angus cattle that have expected progeny difference in the Red Angus Association.

Van Eenennaam et al. 2104. Annual Review Animal Biosciences 2:105-139.



Angus predictions (r) are not very accurate in Red Angus (Data provided by Dorian Garrick)

Trait	Trained in Black Angus/Validated in Black Angus	Trained in Black Angus/Validated in Red Angus
BirthWt	0.64	0.27
WeanWt	0.67	0.28
YearlingWt	0.75	0.23
Fat	0.70	0.21
Rib Eye Area	0.75	0.29
Marbling	0.80	0.21
CalvEase (D)	0.69	0.14
CalvEase (M)	0.73	0.18

Angus = ASREML 5-fold validation Red Angus = correlation Training on de-regressed EPDs Saatchi et al (GSE)

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American Angus Association performs weekly evaluations with genomic data – recently updated to include heifer pregnancy

Association's genetic evaluations, the DNA test results are incorporated into the EPDs using a correlated trait approach.

The correlations (r) between the HD 50K prediction and the phenotypic data at the Association are updated with each recalibration effort and effectively range from .60 to .70, except for milk (.38) and heifer pregnancy (.49).

The December 6, 2013, EPD update includes HD 50K predictions from over 51,000 registered Angus animals with genotypes retained at the Association. Results are incorporated into at least 15 EPDs which are then components of the Angus \$Value selection index suite.

http://www.angus.org/AGI/GenomicCalibrationRelease.pdf December 2013



Other breeds?

The following U.S. breed associations have/are working with Dorian Garrick (IA State) to develop their own 50K-based prediction equations

Breed	Breed code
Hereford	HER
Red Angus	RAN
Simmental	SIM
Brangus	BRG
Limousin	LIM
Gelbvieh	GVH
Maine Anjou	RDP

Van Eenennaam NAAB 9/20/2012





If you are interested in knowing ASA's new product can help.

*For more information. see accompanying article

\$90/sample

Genotyping performed at GENESEEK

Call or email Leoma Wells 406-587-4531 lwells@simmgene.com

16 April 2012

THE FUTURE

Reports Weather Drovers BoVet More Cows Now

proximately a year ago we ran an article in SimTalk to update readers about the state of genomic use in our Industry. The article closed with the following naragraph: Unless you have Angus cattle that are evaluated in the American Angus Association's genetic evaluation, currently available DNA tests are of little to no value to you for EPD enhancement; however, don't be dismayed if you don't fit this description. The recent evolution in genomic technology has spurred organizations to take the steps necessary to harvest its value. For example, ASA is presently working on the development of DNA tests specific to our population, as well as the capacity to incorporate test results into ASA's genetic evaluation."

One year later we are pleased to appounce that the future has arrived at ASA. We are now offering a DNA test that, when incorporated into our genetic evaluation, can add significant enhancement to lower accuracy EPDs. The result of a multiyear collaborative effort, test development was fueled by ASA members and staff, carcass merit cooperators, USDA, University of Illinois, University of Missouri, Montana State University, Gene Seek and the National Beef Cattle Evaluation Consortium

Test development was initiated several years ago throug requests for donated semen on high accuracy stres. ASA mem-bers stepped up to the plate and delivered, with hundreds of DNA samples being collected via donation. Besides older stres, virtually all of the current 500 most heavily used stres were sourced. Samples were also collected on the stres and their offspring fed at the University of Illinois. In total, over 2,700 samples were genotyped. The genotypes, along with the equivalent of millions of phe

notypes (data submitted by breeders and the Carcass Merit Pro-gram over the years) were amassed and analyzed by University of Iowa researchers. The analysis resulted in the parameters required for genetic evaluation.

The multi-tiered effort culminated in a very successful outcome. The standard measure of a DNA test used in EPD prediction is the correlation between test results and the traits of interest. Table 1 displays correlations for ASA's test when used on ASA's population. To provide prospective, correlations for Pfizer and Igenity's tests gleaned from the American Angus Association's website are included in the table.

Table 1. Correlations between DNA test results and trait

Trait	Igenity ^a	Pfizer ^a	ASA
CE	0.47	0.33	0.45
BW	0.57	0.51	0.65
WW	0.45	0.52	0.52
YW	0.34	0.64	0.45
Mlk	0.24	0.32	0.34
MCE	NA	NA	0.32
Stay	NA	NA	0.58
CW	0.54	0.48	0.59
Mrb	0.65	0.57	0.63
REA	0.58	0.60	0.59
BF	0.50	0.56	0.29
SF	NA	NA	0.53



Can I use genomics/DNAinformation to make money?

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AGI DNA Tests	Price	Genomic Tests	Price
Parentage	\$18.00	Zoetis® HD50K (includes Parentage)	\$75.00
Coat Color Test	\$18.00	Add Coat Color	\$5.00
Arthrogryposis Multiplex (AM) Test	\$22.00	Add AM Test	\$8.00
Neuropathic Hydrocephalus (NH) Test	\$22.00	Add NH Test	\$8.00
Contractural Arachnodactyly (CA)	\$22.00	Add CA Test	\$8.00
Test	+==	Add DD Test	\$10.00
Developmental Duplication (DD) Test	\$22.00		1
Myostatin (M1) Test	\$22.00	GeneSeek® GGP-HD (includes Parentage)	\$75.00
Dwarfism (D2) Test	\$22.00	Add Coat Color	\$5.00
		Add AM Test	\$8.00
Additional Sample handling fee of 2.00 will be cl sample for samples submitted in blood tubes or	harged per bair not on	Add NH Test	\$8.00
proper hair cards.		Add CA Test	\$8.00
		Add DD Test	\$10.00
		Add M1 Test	\$18.00
		Add Dwarfism (D2) Test	\$20.00



Compare 20th century response to dwarfism to 21st century response



A Triple Compounded EILEENMERE

Look at the Blood Line Wealth concentrated in one animal. "SHORT SNORTER"



An early '50's advertisement that superimposed a measuring stick in the picture of this bull who was nick-named "Short Snorter."

Based upon his height and age, he was less than a frame score 1.

Image from https://www.msu.edu/~ritchieh/historical/shortsnorter.jpg



From September 8 – November 3, 2008 identified genetic problem, developed test, and released carrier status of 736 bulls!

In the 11 months following the release of the test, the AAA posted the results of tests for AM on about 96,247 cattle.

This amounts to \$2.4 million in testing costs

Of these, 20% (19,529) were carriers of AM. That leaves 23,638 bulls and more than 53,000 heifers which tested as free of AM.

At \$4K/bull and \$2K/heifer ~\$200 million

Based on calculations in Buchanan, D.S. 2009. Genetic Defects in Cattle. <u>http://www.ag.ndsu.edu/williamscountyextension/livestock/genetic-defects-in-cattle</u>



Potential Value of DNA information to the commercial sector

Estimate the value of using DNA test information to increase the accuracy of bull and replacement selection in a commercial herd

The expected returns from using DNA testing to improve the accuracy of selection for

- commercial sires sourced from a seedstock herd
- replacement commercial females.

Van Eenennaam, A. L., J.H. van der Werf, and M.E. Goddard. 2011. The economics of using DNA markers for beef bull selection in the seedstock sector. Journal of Animal Science. 89. 307-320.



Value of improved selection response for commercial bulls due to DNA-test increase in index accuracy

Variable	Unit	Accuracy of DNA test used	\$ Feedlot Index Value
Increased value derived from	\$/	Intermediate	340
ΔG in commercial sires	bull	High	574



Where are returns from genetic gain (AG) realized?



Van Eenennaam Perth 7/22/2011



What is the value of genetic improvement in commercial females?

- The breakeven cost of testing replacement heifers was \$3.63 and \$6.53 per test for the intermediate and high accuracy DNA tests, respectively.
- These values are unique to the hypothetical DNA tests modeled in this study, and are not intended to represent commercial products.
- The value of increasing the accuracy of commercial replacement heifer genetic evaluations is less (ten-fold in this case) than that for comercial bulls because bulls produce more descendants from which to derive returns for accelerated genetic improvement.





Hype cycle: the over-enthusiasm or "hype" and subsequent disappointment that typically happens with the introduction of new technologies

VISIBILITY



Plateau of Productivity

Slope of Enlightenment

Trough of Disillusionment

Technology Trigger

ΤΙΜΕ



Potential uses of genomic information for beef sectors

ONLY THESE SECTORS PRODUCE NEW ANIMALS

Use	Seedstock	Commercial	Feedlot	Processor
DNA-assisted selection	Х	Х		
Parentage	Х	X		
Recessive allele testing	Х	X		
Control of Inbreeding	Х	X		
Mate selection	Х	X		
DNA-assisted management	X	X	Х	
DNA-based purchasing			Х	Х
Product differentiation				Х
Traceability				Х



Ideally cattle would be genotyped ONCE early in life and genotypes shared with downstream production sectors to derive the maximum value from the fixed DNA collection and extraction costs

Cattle industry	Type of DNA product //	Cost??
Sector	required	
Nucleus seedstock/AI bulls	Full genome sequence	\$250
Seedstock/bull multiplier	HD 770 K genotype	\$50
Registered females and stock bulls for commercial sector	50K genotype + parentage + single gene traits/recessives	\$25
Commercial cattle – Marker- assisted management (MAM), replacement heifer selection	Imputation LD chip + parentage + single gene traits/recessives	\$10
Feedlot cattle purchasing, sorting and marker-assisted management (MAM)	Access genotypes from supplier (subset of LD imputation chip).	<\$1
Traceability for voluntary labelling e.g. Angus beef	Access genotypes from supplier (subset of LD imputation chip).	<\$1
Traceability for disease outbreak/contaminated meat	Access genotypes from supplier (subset of LD imputation chip).	<\$1







2003

2008



2020

 multimarker tests for a few traits reported in a variety of formats no tie between DNA test results and national genetic evaluation or breed

associations tests accounted

- for < 10% additive genetic variation
- limited validation
- technology not in a form producers could use

- panels with thousands of markers for many traits
- results reported in units of the trait
- incorporation of DNA information into national genetic evaluation
- DNA-based evaluations improve accuracy of EPDs
- large numbers of genotyped populations being developed for hard to measure traits

- universal causative SNP marker panel used by worldwide beef cattle community
- seamless submission of genotype data to national genetic evaluation/breed associations
- testing cost is low
- DNA information used for traceability, parentage, genetic defects, selection, marker-assisted management, product differentiation

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CONCLUSION: Ramifications of DNA-enabled selection

- The benefits of genomic selection are best captured in well-structured industries (e.g. dairy/poultry/swine) that are already making significant genetic progress
- May encourage more vertical integration to collect phenotypes to enable predictions for EPDs for all sectors
- May see genetic evaluations developed for novel traits e.g. feed efficiency, disease resistance if large enough populations can be amassed and data shared
- May see breeds/countries start to share data especially with whole genome sequencing and causative SNP
- This technology might accelerate vertically-integrated breeding companies owning all sectors of industry



Concluding thought....

Breeds/groups that can organize themselves and technologically and structurally to seamlessly obtain and marry entire supply chain phenotypes and genotypes and take advantage of the rapidlydeclining cost of genotyping to capture the cumulative value derived from using genomic information for multiple purposes (selection, parentage, genetic defects, marker-assisted management, product differentiation, traceability) will be ideally positioned to fully realize the nascent potential of genomic information.

Van Eenennaam, A. L., and D. J. Drake. 2011. Where in the beef cattle supply chain might DNA tests generate value? Animal Production Science. 52(3) 185-196.

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Thanks for inviting me!







National Research Initiative competitive grant no. 2009-55205-05057 ("Integrating DNA information into beef cattle production systems") from the USDA National Institute of Food and Agriculture Animal Genome Program.



United States Department of Agriculture

National Institute of Food and Agriculture

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Questions?

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USDA funded projects – competitive call for proposals: Part 2 (new NIFA AFRI proposals)

- National program for genetic improvement of feed efficiency in beef cattle
 - (Taylor, MO) finishes 4/2016 (http://www.beefefficiency.org)
 - Genotype ~ 2,400 head on HD chips; 7000 records FE records
 - \$5 million, 5 year project; April 2011 April 2016
- Integrated program for reducing bovine respiratory disease (BRD) in beef and dairy cattle (Womack, TX) – finishes 4/2016 (<u>http://www.brdcomplex.org</u>)
 - Collection and HD genotypes on 6,000 BRD case-control animals
 - \$10 million, 5 year project; April 2011 April 2016
- Identification and management of alleles impairing heifer fertility while optimizing genetic gain in Angus cattle (Patterson, Taylor, et al. MO; Van Eenennaam, CA) – finishes 12/17
 - Sequence up to 250 cattle from up to 10 different beef breeds
 - \$3 million, 5 year project; Jan 2013 December 2017