

# VALIDATION AND ESTIMATION OF ADDITIVE GENETIC VARIATION ASSOCIATED WITH DNA TESTS FOR QUANTITATIVE BEEF CATTLE TRAITS



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There are various companies offering DNA tests for marker-assisted selection in beef cattle



# The past

- Single marker tests
- Genotypes reported directly (Stars or “TT”)
- Validation asked “Is there an association between the marker and the target trait?”

### Igenity™ L. Know. Now.

#### Advanced technology. Advanced knowledge.

What if there was a test that could tell you – in advance – an animal's genetic potential for energy utilization or carcass quality? You'd have the advantage of knowing an animal's potential now, instead of discovering it later through success or failure in the milk string or when the animal goes to market.

Researchers have discovered the specific gene that carries the code for the production of a protein called *leptin*. Leptin is associated with an animal's potential for appetite and energy utilization, among other things.


- For *dairy cattle* this translates directly into maximum dry matter intake (DMI) and peak milk production.
- For *beef cattle* it relates to days on feed and carcass quality.


The IGENITY™ L Test identifies leptin genotype (L-tt™, L-ct™ or L-cc™). Now you have another important resource to help you breed, feed, sort, manage and market cattle at an optimum level.

- Leptin is involved in the regulation of feed intake, energy balance, milk production, milk components, marbling scores, puberty, fertility and immune functions.
- Knowing an animal's leptin genotype empowers you to make more informed, strategic management decisions regarding breeding and nutrition.
- The IGENITY L Test identifies an animal's leptin genotype at the DNA level, with 100% accuracy.

Market your cattle with  
the IGENITY L logo system:

 L-tt™

 L-ct™

 L-cc™



# A lot of detail about the marker

Igenity™ L. Know. Now.

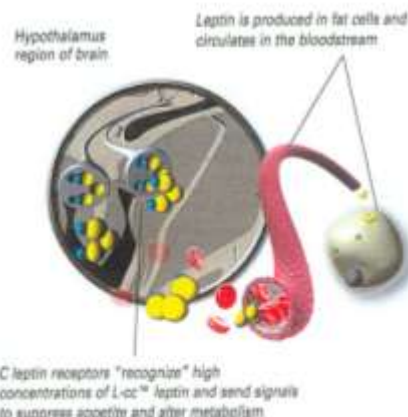
## Introduction to the Leptin Protein in Cattle

- Leptin is a protein that influences appetite and metabolism (energy storage and utilization).
- Leptin is produced by fat tissue stored by the body as energy reserves. The more fat tissue, the higher the leptin concentration circulating in the blood.
- High concentrations of leptin normally signal the brain to suppress appetite and draw on stored energy for maintenance.
- Certain types of leptin are not easily recognized by the brain, so appetite and metabolism are not changed.
- The IGENITY™ L Test can identify the genetic variation that determines what type of leptin an animal will produce.

### The function of leptin.

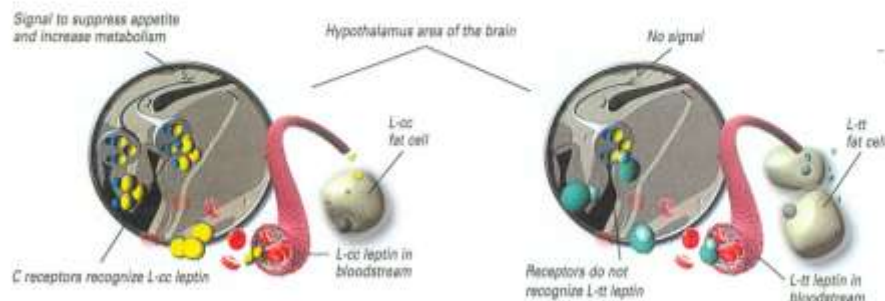
- Leptin is the centerpiece of an important negative feedback system involving key metabolic regulators, including insulin, glucocorticoids and the sympathetic nervous system.
- The word "leptin" comes from the Greek word *leptos*, meaning "thin."
- Genotype determines what type of leptin is produced by fat tissues and, to a lesser extent, the type of leptin receptors that operate in the hypothalamus.

- Leptin is involved in a feedback system involving the hypothalamus region of the brain:
  - When leptin receptors recognize high concentrations of leptin, they send signals to suppress appetite and increase metabolism.
  - If high leptin levels are not recognized, the animal senses hunger and the system focuses on storing energy in many forms, including intramuscular fat.
- The gene that carries the code for leptin production has been called the "obese" gene or "marbling" gene because of leptin's association with appetite and fat deposition.
- When cytosine (c) is present at the gene sites for leptin production, normal leptin results. When thymine (t) is present, this changes the amino acid structure of leptin – disguising it.
- If an animal has one chromosome with a "c" at the critical site and one containing a "t," then it creates both types of leptin.
- The science behind the IGENITY L Test identifies leptin genotype and provides valuable knowledge for feeding and breeding decisions.



## Not All Leptin is Created Equal

Igenity™ L. Know. Now.



### Activity of L-cc™ Leptin and Receptors

- As L-cc leptin proteins reach the blood-brain barrier, receptors recognize them.
- If concentration is high, a signal is sent to suppress appetite.

### Activity of L-tt™ Leptin and Receptors

- The L-tt leptin is structurally different and is more difficult for receptors to recognize. As a result, there is no signal to reduce appetite.
- L-ct™ cattle produce both types of leptin – some normal, some difficult to recognize.

### Leptin Genotype. It pays to know now.

- Identifying leptin genotype – and selectively breeding for desired leptin genotype – can have a great impact on a dairy or beef operation.
- The benefits can extend beyond increased milk production or beef marbling to greater management options for ration selection and transition cow nutrition, or beef finishing and marketing strategies.
- The beneficial result is that cattle with the L-tt genotype remain in a "hunger" mode and are predisposed to consume more feed:

- In dairy cattle, this can result in greater dry matter intake (DMI), greater peak lactation, improved body condition scores and improved energy utilization (less time spent in negative energy balance).
- In beef cattle, this can result in greater DMI and superior marbling.
- On the other hand, L-cc genotype cattle will tend to have lower DMI at critical phases, such as the first 100 days of lactation in dairy cows, or the final 60 days on feed for beef cattle.
- The science behind the IGENITY L Test provides a simple DNA test to identify leptin genotype with 100% accuracy.



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igenity™ L

Know. Now.

## Advanced technology. Advanced knowledge.

What if there was a test that could tell you – in advance – an animal's genetic potential for energy utilization or carcass quality? You'd have the advantage of knowing an animal's potential now, instead of discovering it later through success or failure in the milk string or when the animal goes to market.

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- For *dairy cattle* this translates directly into maximum dry matter intake (DMI) and peak milk production.
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The IGENITY™ L Test identifies leptin genotype (L-tt™, L-ct™ or L-cc™). Now you have another important resource to help you breed, feed, sort, manage and market cattle at an optimum level.

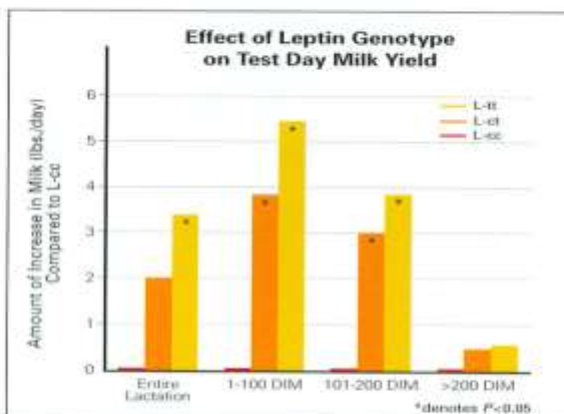
## For the dairy producer.

The science behind IGENITY L lets you identify genetic ability for:

- increased dry matter intake (DMI)
- greater peak and overall lactation yield with increased protein solids
- improved body condition scores
- superior energy utilization
- quicker return to positive energy balance.

In trials, L-tt cows outperform L-cc cows:<sup>1</sup>

- entire lactation – 3.3 lbs more milk/day
- first 100 days – 5.38 lbs more milk/day.



SOURCE: Buchanan, et al. 2003. An Association Between a Leptin Single Nucleotide Polymorphism and Milk and Protein Yield. *Journal of Dairy Science* 86:3164-3166.

Use IGENITY L to:

- Select bulls to improve the leptin profile of your herd.
- Select cows and replacement heifers with the greatest potential.
- Sort and feed for optimum early lactation performance.

## For the beef producer.

The IGENITY L Test helps you identify genetic potential for:

- greater DMI
- superior marbling ability
- more efficient energy utilization.

In trials through to slaughter:

- Cattle with higher leptin concentrations had higher marbling scores.<sup>2</sup>
- Cattle with L-tt leptin were up to 5 times more likely to grade Choice than cattle identified as L-cc.<sup>3</sup>

## Effect of Genotype on Carcass Quality

	L-cc	L-ct	L-tt	P-value
Trial 1 - % Choice	11	29	62	0.03
Trial 2 - % Choice	0	19	48	0.01
Trial 3 - % Choice	38	45	58	0.07

Trial 1: AzTx Feeders (Charolais/Angus steers), Trial 2: Doerksen Feedlot (Hereford steers), Trial 3: University of Saskatchewan (Charolais steers)  
SOURCE: Quantum Genetics, Inc.

IGENITY L can help you:

- Buy L-tt bulls to improve your herd's potential for marbling.
- Retain cows and select replacement heifers with desired leptin genotype, along with other genetic traits.
- Breed, feed and sort cattle so they reach targeted endpoints uniformly and efficiently.



## Commercial genetic test validations

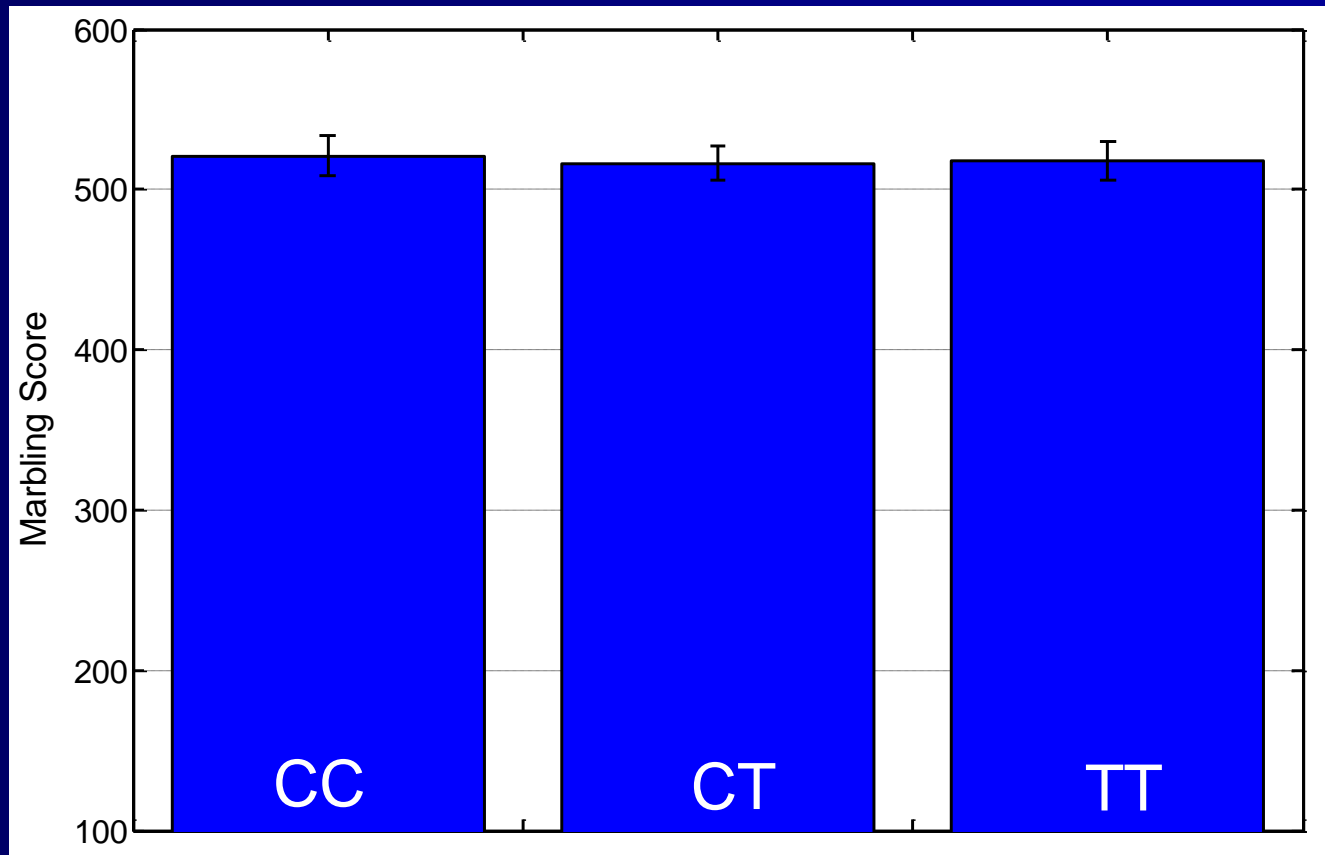


The purpose of the NBCEC commercial DNA test validation is to independently verify associations between genetic tests and traits as claimed by the commercial genotyping company using phenotypes and DNA from reference cattle populations

The validation process is a partnership of the owners of DNA and phenotypes (e.g., breed associations) and genomics companies, facilitated by the NBCEC

A. L. Van Eenennaam, J. Li, R. M. Thallman, R. L. Quaas, M. E. Dikeman, C. A. Gill, D. E. Franke, M. G. Thomas. 2007. Validation of commercial DNA tests for quantitative beef quality traits. *Journal of Animal Science*. 85:891-900.

# Leptin Genotype Effects on Marbling Score (NBCEC Data)



Data provided by R. L Quass, Cornell University



# The present

- Multimarker tests for a few traits reported in a variety of formats (MVPs, MBVs, 1-10)
- No tie between DNA test results and national genetic evaluation
- Independent assessments suggest tests account for a small proportion of additive genetic variation – variable results
- Results presented alongside EBVs

## Commercial genetic test validations

[Overview](#)[Pfizer Animal Genetics \(Bovigen\)](#)[IGENITY](#)[MMI Genomics](#)[Ancillary Results](#)

**Summary of NBCEC validations for commercially-available DNA-tests for complex (quantitative or multigenic) traits in beef cattle** (note: validations do not include tests for "simple" traits such as coat color, horned/polled, AM status etc.)

Company	Test Name	Trait	Date of validation
<b>Igenity</b> <a href="http://www.igenity.com">www.igenity.com</a>	Profile®	<a href="#">Fat Thickness</a>	12/2008
	Profile®	<a href="#">Marbling Score</a>	12/2008
	Profile®	<a href="#">Quality Grade</a> (% ≥ Choice)	12/2008
	Profile®	<a href="#">Rib Eye Area</a>	12/2008
	Profile®	<a href="#">Yield Grade</a>	12/2008
	Profile®	<a href="#">Average Daily Gain</a>	12/2008
	Profile®	<a href="#">Tenderness</a>	12/2007
	Profile®	<a href="#">Residual Feed Intake</a> (RFI) (for <i>Bos indicus</i> influenced cattle)	12/2007
	Profile®	<a href="#">Residual Feed Intake</a> (RFI) (for <i>Bos taurus</i> cattle)	6/2008
	Profile®	<a href="#">Dry matter intake</a> (DMI) (for <i>Bos indicus</i> influenced cattle)	12/2007
	Profile®	<a href="#">Heifer Pregnancy Rate</a>	
	Profile®	<a href="#">Stayability</a> (longevity)	
	Profile®	<a href="#">Maternal Calving Ease</a>	
	Profile®	<a href="#">Docility</a>	
<b>Pfizer Animal Genetics</b> (Bovigen) <a href="http://www.bovigen.com">www.bovigen.com</a>	GeneSTAR® Tenderness MVP	<a href="#">Tenderness</a>	2/2009
	GeneSTAR® Marbling MVP	<a href="#">% IMF</a> (Feedlot cattle)	2/2009
	GeneSTAR® Feed Efficiency MVP	<a href="#">Net Feed Intake</a> (NFI)	2/2009
<b>MMI genomics</b> <a href="http://www.metamorphixinc.com">www.metamorphixinc.com</a>	Tru-Marbling™	<a href="#">Marbling Score and Quality Grade</a>	
	Tru-Tenderness™	<a href="#">Tenderness</a>	

## IGENITY profile Feed Efficiency for Bos taurus cattle SUMMARY

The IGENITY TAURUS feed efficiency MBVs were inconsistently associated with residual feed intake in the validation populations. In two populations there was a significant positive association of the MBV with the trait (North American Bos Taurus, CRC Temperate), but in the remaining four populations there was no significant effect and in both Angus populations the estimated association was negative, meaning that the results were associated in the opposite direction.

For further information on this validation contact Dr. John Pollak (607) 255-2846.

TEST DATASET	Trait	PANEL	b	P	N
TEMPERATE <sup>1</sup> (CRC1)	RFI	TAURUS	0.309	0.04	~546
SHORTHORN <sup>1</sup> (CRC)	RFI	TAURUS	0.393	0.17	~189
ANGUS (CRC) <sup>1</sup>	RFI	TAURUS	-0.426	0.95	~327
NORTH AMERICAN BOS TAURUS <sup>2</sup>	RFI	TAURUS	0.351	0.005	~706
NORTH AMERICAN CHAROLAIS <sup>3</sup>	RFI	TAURUS	0.022	.443	~393
NORTH AMERICAN ANGUS <sup>3</sup>	RFI	TAURUS	-0.217	0.89	~436

<sup>1</sup> Data analyses for these validation populations were performed by Dr. David Johnston, Animal Genetics and Breeding Unit, University of New England, Armidale, Australia (6/2008).

<sup>2</sup> Data analyses for this validation population was performed by Gordon VanderVoort, Dr. Matt Kelly, Duc Lu and Dr. Stephen Miller, University of Guelph (6/2008)

<sup>3</sup> Data analyses for these validation populations were performed by Dr. Denny Crews, Agriculture and Agri-Food Canada (6/2008)





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## Australian beef DNA results

As part of its role in delivering DNA markers to the Australian beef industry, Beef CRC has agreed to independently test new panels of DNA markers as they are commercialised by companies such as Pfizer Animal Genetics, Igenity /Merial and Metamorphix Inc.

Results of all independent testing of commercially-available DNA markers undertaken by Beef CRC will be presented on this site, outlining the size and direction of effect and the amount of genetic variation that is accounted for by each panel of markers for the different traits (e.g. marbling, feed efficiency, tenderness etc).

Additional information is provided to help beef businesses interpret the results for themselves to determine the value to their own businesses from an investment in the particular panel of DNA markers.

Those decisions very much depend on the individual business' attitude to risk and can only be made effectively by the individual business.

It is possible that the panel of markers has also been independently evaluated in North American herds by the US National Beef Cattle Evaluation Consortium, so for further information on the size and direction of effect of the markers in those populations, please visit <http://www.ansci.cornell.edu/nbcec/>

[Pfizer GeneStar results](#)

[Pfizer interpretation](#)

## Success Stories

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ivariate animal model results using all phenotypes and GeneSTAR MVPs from the 56 marker panel Version January 2009.  $\sigma^2_p$  = phenotypic variance of the observed data after fitting the models,  $h^2$  = heritability of the trait, note MVP have a heritability fixed close to 1.0,  $r_g$  = genetic correlation between MVP and target trait,  $r_m^2$  = portion of genetic variance explained by marker,  $b$  = regression coefficient of MVP on phenotype. Standard errors of  $b$  are in brackets,  $P$  = significant level of regression coefficient ( $b$ ) being greater than zero,  $r_p$  = correlation between MVP and phenotypes

		Phenotypic parameters						Genetic Parameters		
Trait	Data	N	$\sigma^2_p$	$b$ (se)	P	$r_p$	$r_m^2$	$h^2$ (se)	$r_g$ (se)	$r_m^2$
IMF	1	Phenot = 3,594 MVP = 703	2.035 0.035	0.255 (0.30)	0.20	0.033 (0.04)	0.001 (0.003)	0.39 (0.06)	0.054 (0.06)	0.003 (0.007)
	2	Phenot = 3,524 MVP = 668	0.978 0.027	0.231 (0.24)	0.17	0.038 (0.04)	0.001 (0.003)	0.37 (0.06)	0.064 (0.07)	0.004 (0.009)
	3	Phenot = 876 MVP = 253	0.767 0.026	0.028 (0.33)	0.47	0.005 (0.06)	0.000 (0.001)	0.23 (0.10)	0.011 (0.13)	0.000 (0.003)
	4	Phenot = 878 MVP = 225	0.717 0.022	0.415 (0.39)	0.14	0.072 (0.07)	0.005 (0.010)	0.37 (0.11)	0.121 (0.11)	0.015 (0.027)
MSA MS	1	Phenot = 1,454 MVP = 710	0.281 0.035	0.218 (0.20)	0.14	0.077 (0.07)	0.006 (0.011)	0.35 (0.09)	0.131 (0.12)	0.017 (0.031)
	2	Phenot = 1,808 MVP = 670	0.236 0.027	0.171 (0.15)	0.13	0.057 (0.05)	0.003 (0.006)	0.37 (0.08)	0.096 (0.08)	0.009 (0.015)
	3	Phenot = 594 MVP = 253	0.211 0.026	0.024 (0.22)	0.46	0.009 (0.08)	0.000 (0.001)	0.31 (0.13)	0.016 (0.14)	0.000 (0.004)
	4	Phenot = 636 MVP = 225	0.229 0.022	0.262 (0.23)	0.13	0.080 (0.07)	0.006 (0.011)	0.19 (0.11)	0.189 (0.17)	0.036 (0.064)
LDSF	1	Phenot = 3,322 MVP = 659	0.433 0.088	0.240 (0.20)	0.11	0.049 (0.04)	0.002 (0.004)	0.08 (0.04)	0.170 (0.14)	0.029 (0.048)
	2	Phenot = 3,254 MVP = 585	0.612 0.160	0.662 (0.20)	<0.001	0.154 (0.04)	0.024 (0.012)	0.30 (0.06)	0.283 (0.08)	0.080 (0.045)
	3	Phenot = 785 MVP = 253	0.658 0.142	0.304 (0.35)	0.19	0.064 (0.07)	0.004 (0.009)	0.26 (0.10)	0.126 (0.14)	0.016 (0.035)
	4	Phenot = 762 MVP = 225	0.871 0.142	1.658 (0.40)	<0.001	0.302 (0.07)	0.091 (0.042)	0.31 (0.10)	0.547 (0.13)	0.299 (0.142)
NFI	1	Phenot = 785 MVP = 706	0.840 0.079	0.300 (0.13)	0.01	0.092 (0.04)	0.008 (0.007)	0.14 (0.11)	0.248 (0.15)	0.062 (0.074)
	2	Phenot = 687 MVP = 671	0.687 0.056	0.366 (0.15)	0.01	0.104 (0.04)	0.011 (0.008)	0.21 (0.13)	0.232 (0.11)	0.054 (0.051)
	3	Phenot = 254 MVP = 253	1.110 0.082	-0.074 (0.27)	0.81	-0.020 (0.07)	0.000 (0.003)	0.21 (0.25)	-0.044 (0.16)	0.002 (0.014)
	4	Phenot = 215 MVP = 225	0.958 0.056	-0.131 (0.33)	0.86	-0.032 (0.07)	0.001 (0.004)	0.37 (0.26)	-0.053 (0.14)	0.003 (0.015)

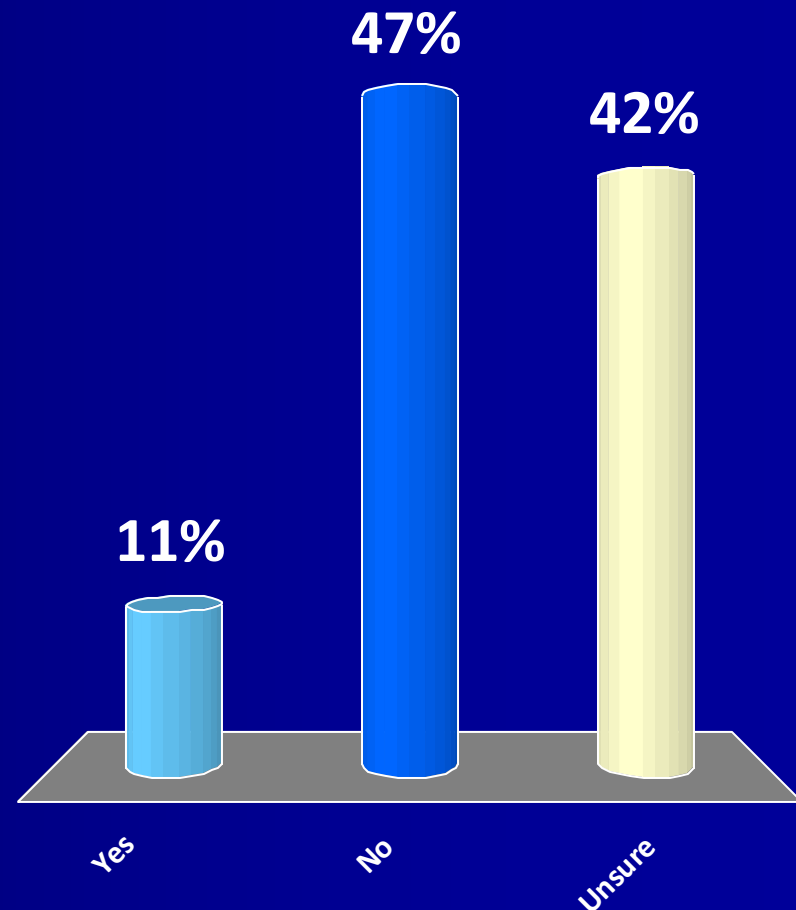
**Proportion of genetic variance explained by DNA-tests that have been independently assessed by AGBU in Australia. The test was not predictive ( $p < 0.05$ ) of the target trait in cells that are not shaded.**

Population	IMF%	MSA Marble Score	SF (kg)	NFI (kg)
1. <i>Bos taurus</i>	0.3%	1.7%	2.9%	6.2%
2. <i>Bos indicus</i>	0.4%	0.9%	8.0%	5.4%
3. <i>Bos taurus</i> x <i>Bos indicus</i>	0%	0%	1.6%	0%
4. <i>Bos indicus</i> X Brahman	1.5%	3.6%	29.9%	0%



**Would you use a test that explains a proportion ranging from 0 to 0.15 of the additive genetic variation associated with the target trait, has a regression coefficient of 0.26 ( $\pm 0.3$ ), and a  $p$  value of 0.001?**

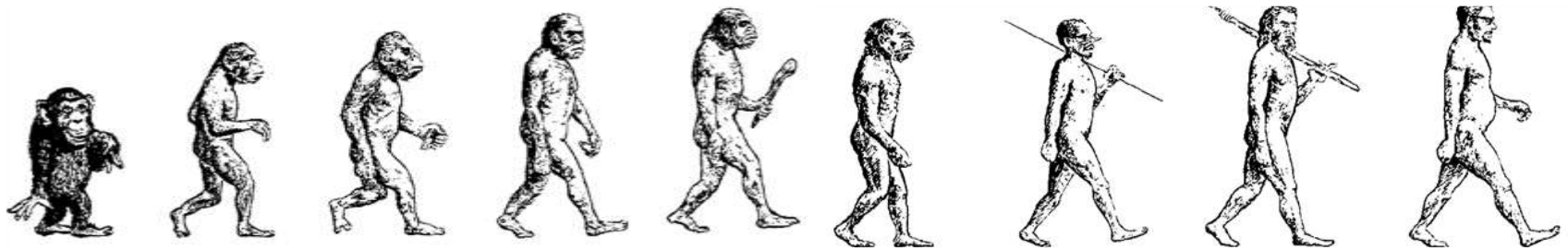
1. Yes
2. No
3. Unsure



# The future

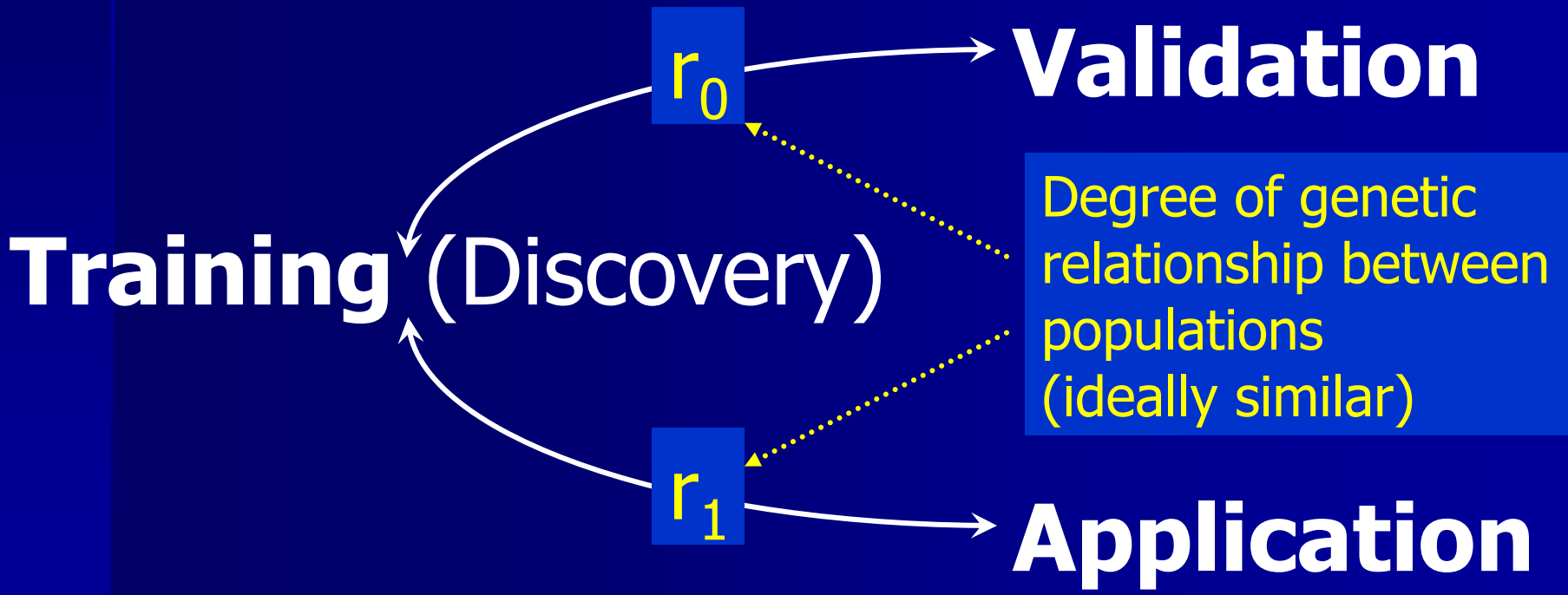
- Panels with hundreds-thousands of markers for more traits derived from 50K data

- ??????????





**Validation:** Purpose is to estimate the correlation between the prediction and the true genetic merit.





# Model for Applying Whole Genome Selection to Beef Cattle

$r_0$

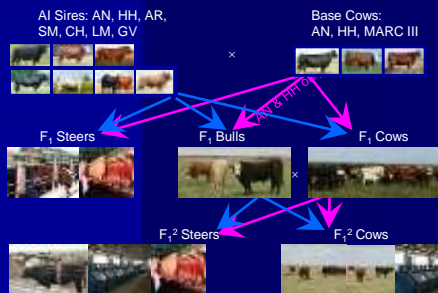
**Validation:**  
2,000 Bull Project  
International Collaboration

**Training:**  
USMARC Cycle VII  
USMARC Ongoing GPE  
DNA Testing Companies  
Seedstock Field Data  
(where applicable)



$r_1$

**Application:**  
Seedstock Breeders



# 2000 Bull Project



- Collaborative Effort
  - Researchers
  - Breed Associations
- Breed associations provided semen for DNA on influential sires
- USMARC ran the 50K SNP chip on those 2,000 sires
- USMARC provides extensively phenotyped animals for use as training data set

# 2,000 Bull Project: Number of Sires Sampled



• Angus 402



• Hereford 317



• Simmental 253



• Red Angus 173



• Gelbvieh 136



• Limousin 131



• Charolais 125



• Shorthorn 86



• Brangus 68



• Beefmaster 64



• Maine-Anjou 59



• Brahman 53



• Chiangus 47



• Santa Gertrudis 43



• Salers 42



• Braunvieh 27

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2026



# Beef information nucleus (BIN) for Australian beef cattle breeds

- Structured progeny test to measure BREEDPLAN traits (plus optional NFI, EQ and lifetime female reproduction)
- DNA collected on all animals
- Provides assessment populations for DNA markers relative to Australian breeds and production systems
- Provides the information to enable combination of molecular data with pedigree and phenotypes to produce BREEDPLAN marker assisted EBVs (EBV<sup>M</sup>s)
- Part of the CRC/MLA Strategic plan for DNA Marker commercialisation
- MLA Donor Company is offering to match 50:50 funding

# CONCLUSIONS

- Validation moving from a pass/fail association to an assessment of the correlation between the test results and true genetic merit.
- Currently there is a paucity of phenotyped populations – worldwide
- Beef information nucleus (BIN) has been proposed as a model to address this issue and develop BREEDPLAN marker assisted EBVs (EBV<sup>M</sup>s) for Australian breeds and production systems

