WILL DNA TESTING MAKE ME MONEY?

Alison Van Eenennaam
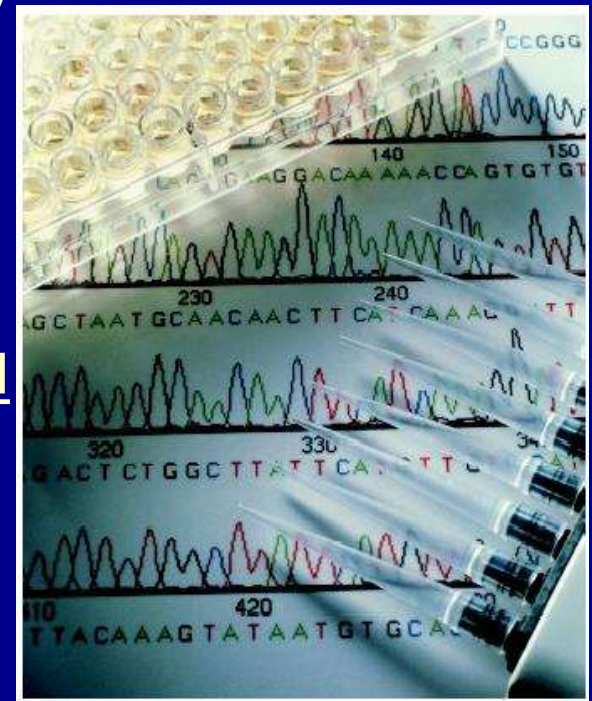
Animal Genomics and Biotechnology

Cooperative Extension Specialist

Department of Animal Science

University of California, Davis

USA

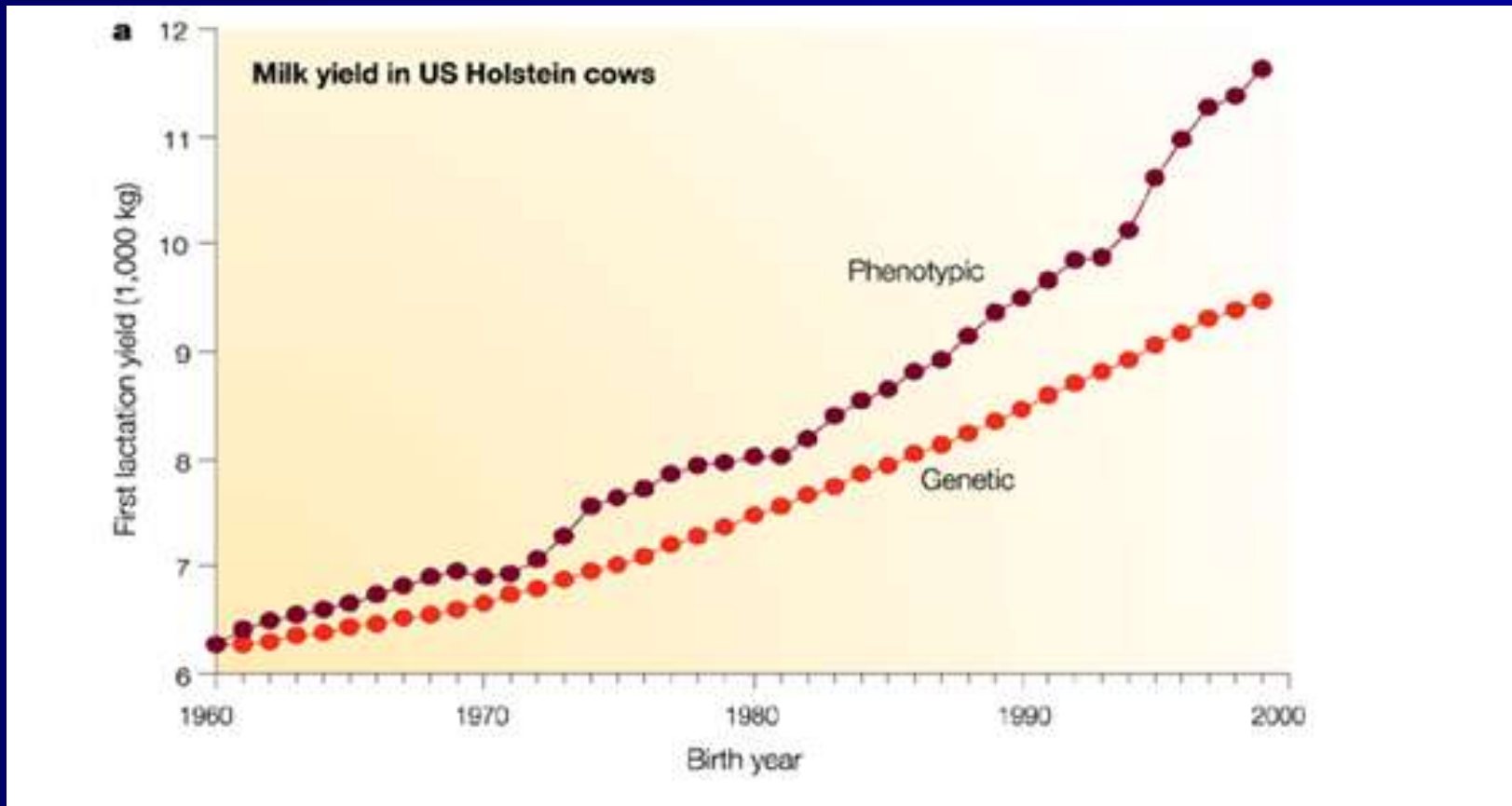alvaneenennaam@ucdavis.edu

animalscience.ucdavis.edu/animalbiotech

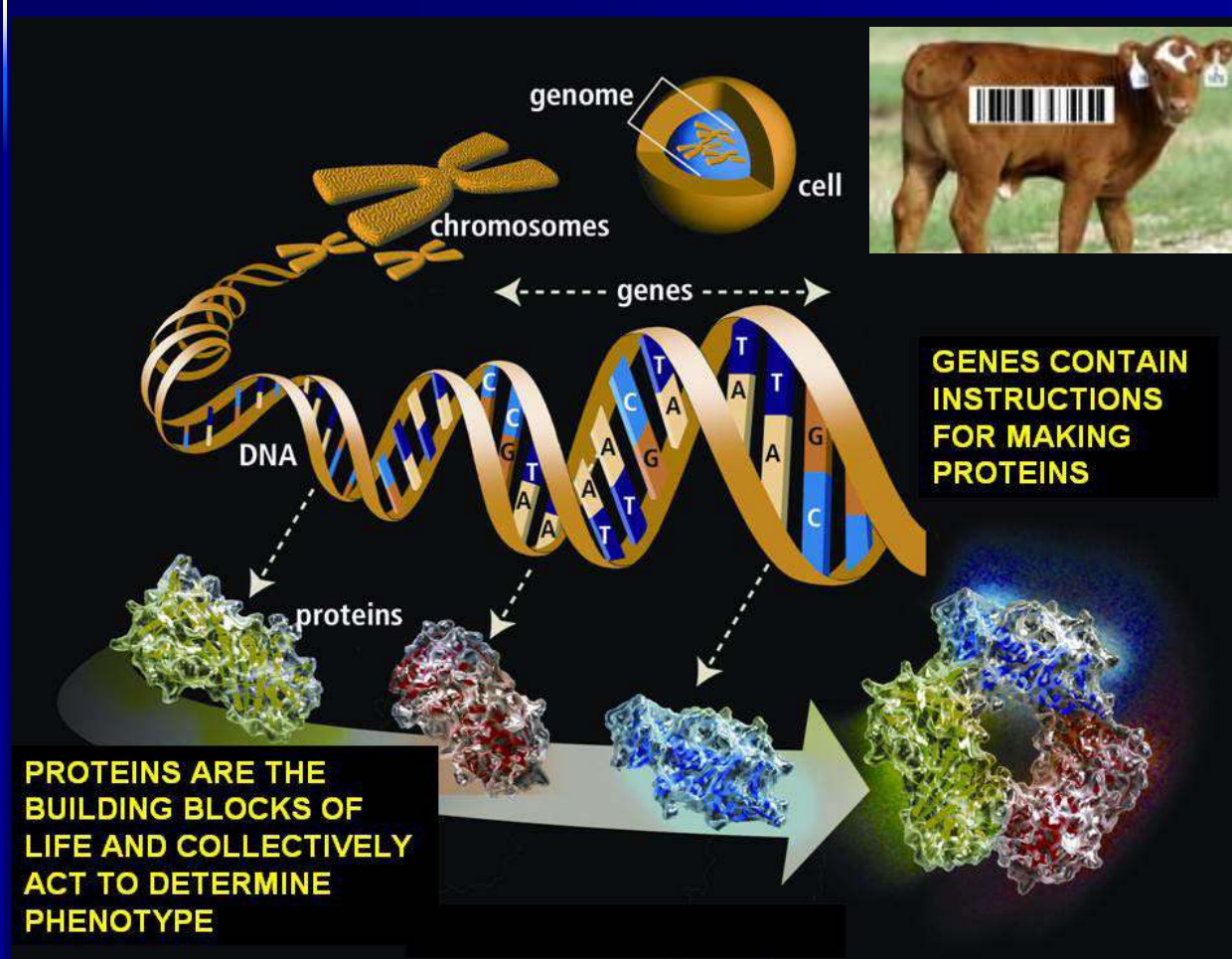# Animal breeders have used selection based on appearance to great effect!

Objective performance recording has accelerated the rate of genetic progress

Milk yield in US Holstein cows

The bovine genome sequence has opened up the possibility of using DNA information or genotypes for selection

genome

cell

chromosomes

genes

GENES CONTAIN INSTRUCTIONS FOR MAKING PROTEINS

DNA

proteins

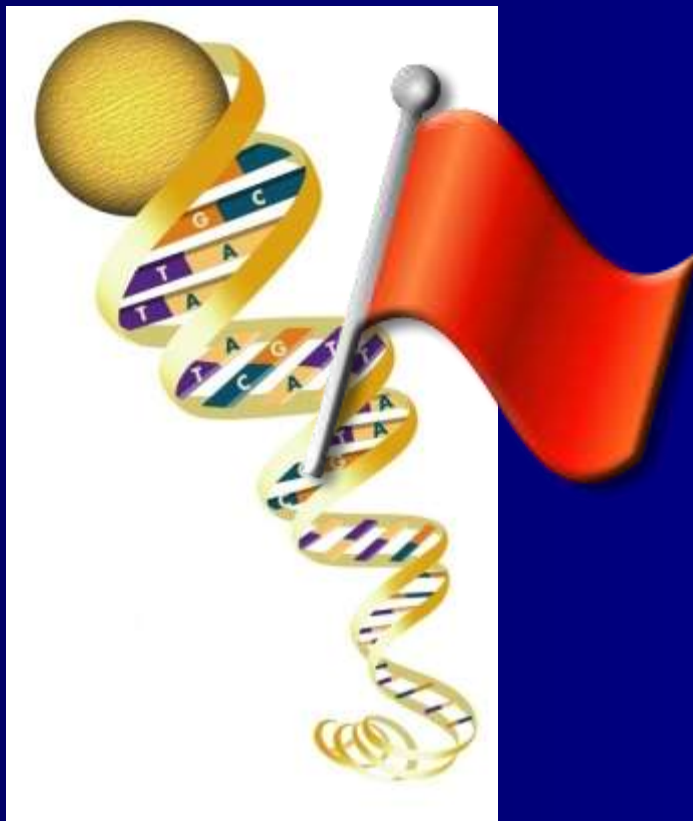PROTEINS ARE THE BUILDING BLOCKS OF LIFE AND COLLECTIVELY ACT TO DETERMINE PHENOTYPE

Human & cattle genomes are 83% identical

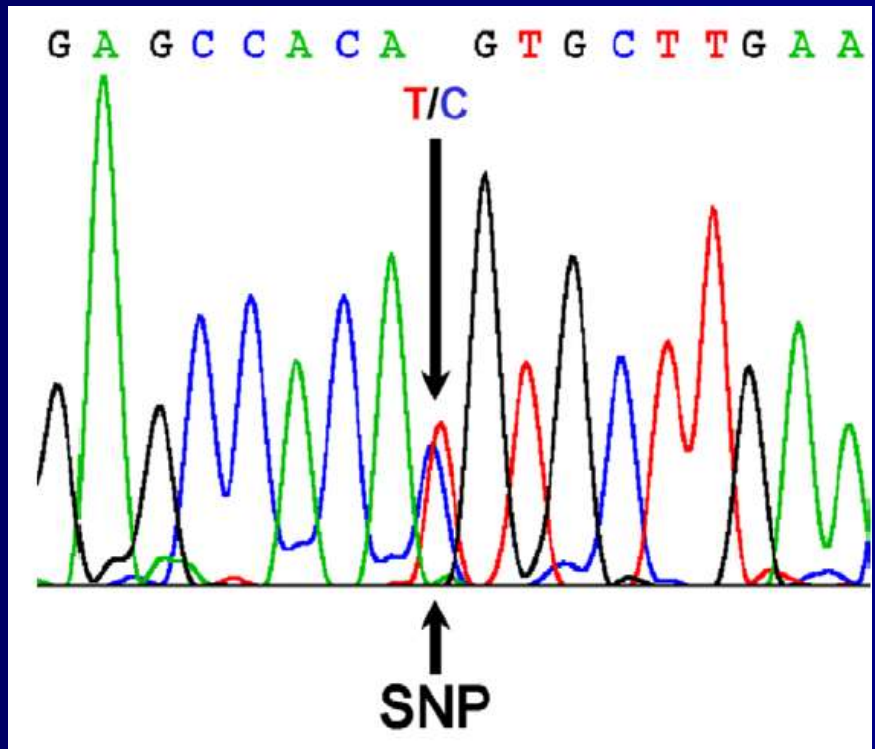# What is a Genetic Marker ?
A DNA sequence variation that has been associated with a given trait in one or more populations

SNPs = Single nucleotide polymorphisms (pronounced SNIPS)

SNPs are the most common and stable type of DNA marker in cattle and are ideally suited for automated, economical genetic testing

Carrier bull

CATGT

CACGT

½   ½
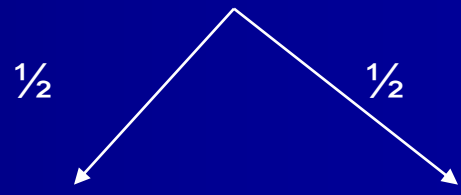
...CATGT…   …CACGT…

What can DNA information be used for?

– Parentage

– Identification of recessive/single trait defects

– Dairy marker-assisted selection

– Beef marker-assisted selection

- **What DNA tests are out there?**
- **Can DNA testing make me money?**

California Commercial Beef Producer Collaboration
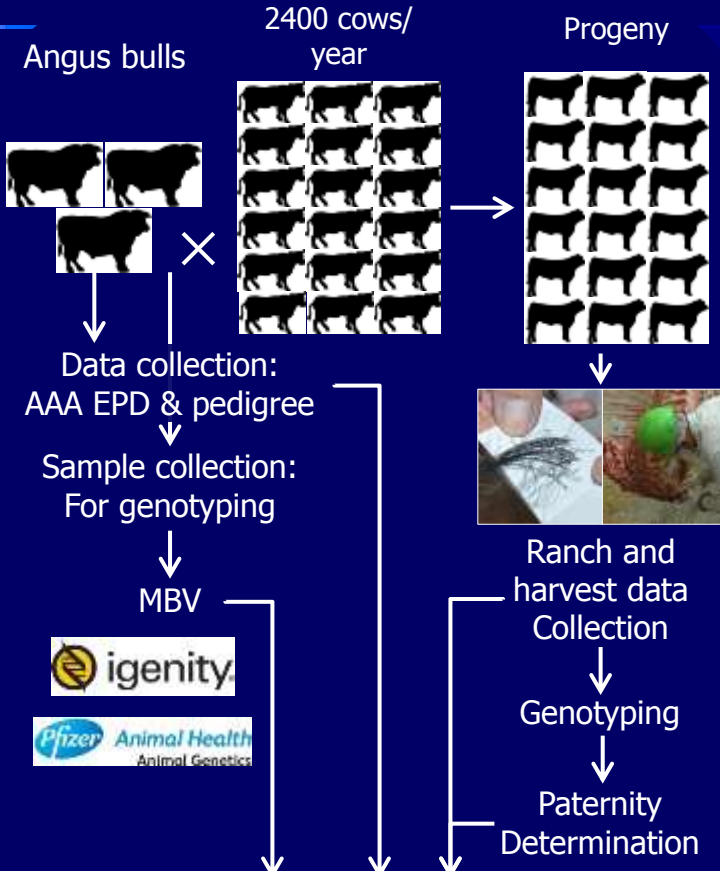
Angus bulls

2400 cows/year

Progeny

×

Data collection:
AAA EPD & pedigree

Sample collection:
For genotyping

MBV

igenity

Pfizer Animal Health
Animal Genetics

Ranch and harvest data Collection

Genotyping

Paternity Determination

Assessment of DNA-enabled approaches for predicting the genetic merit of herd sires on commercial beef ranches

Four ranches:
- Cowley (900 cows)
- Kuck (500 cows)
- Mole-Richardson (700 cows)
- UC Davis (300 cows)

Approximately 125 Angus bulls, and 2,400 cows per year on project

USDA

NIFA

United States Department of Agriculture
National Institute of Food and Agriculture

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What does a California Commercial Ranch collaborator look like?

Photo taken in 1949 at Red Bluff Bull Sale, CA Generously provided by Cathy Maas from Crowe Hereford Ranch, Millville, CA.

Cowley Ranch

Kuck Ranch

Mole-Richardson Farms

A key issue in commercial situations is ease of DNA sampling, tracking and quality of resultant DNA

# Advantages of DNA-based parentage identification

- Correct pedigree errors so improve the rate of genetic gain
- Enables the use of multi-sire breeding pasture
  - Higher fertility
  - Elimination of sire failure
  - Tighter calving season
- Reduces the need for different breeding pastures
  - Allows for better pasture management
  - Less sorting and working of animals into different groups
- No need to interrupt disturb calf/dam bonding after birth
- Enables the development of commercial-ranch genetic evaluations
  - Can determine which bull is causing calving problems

Calf output per bull

# of calves born/bull – Fall 2009 calving

Late (61+ days)
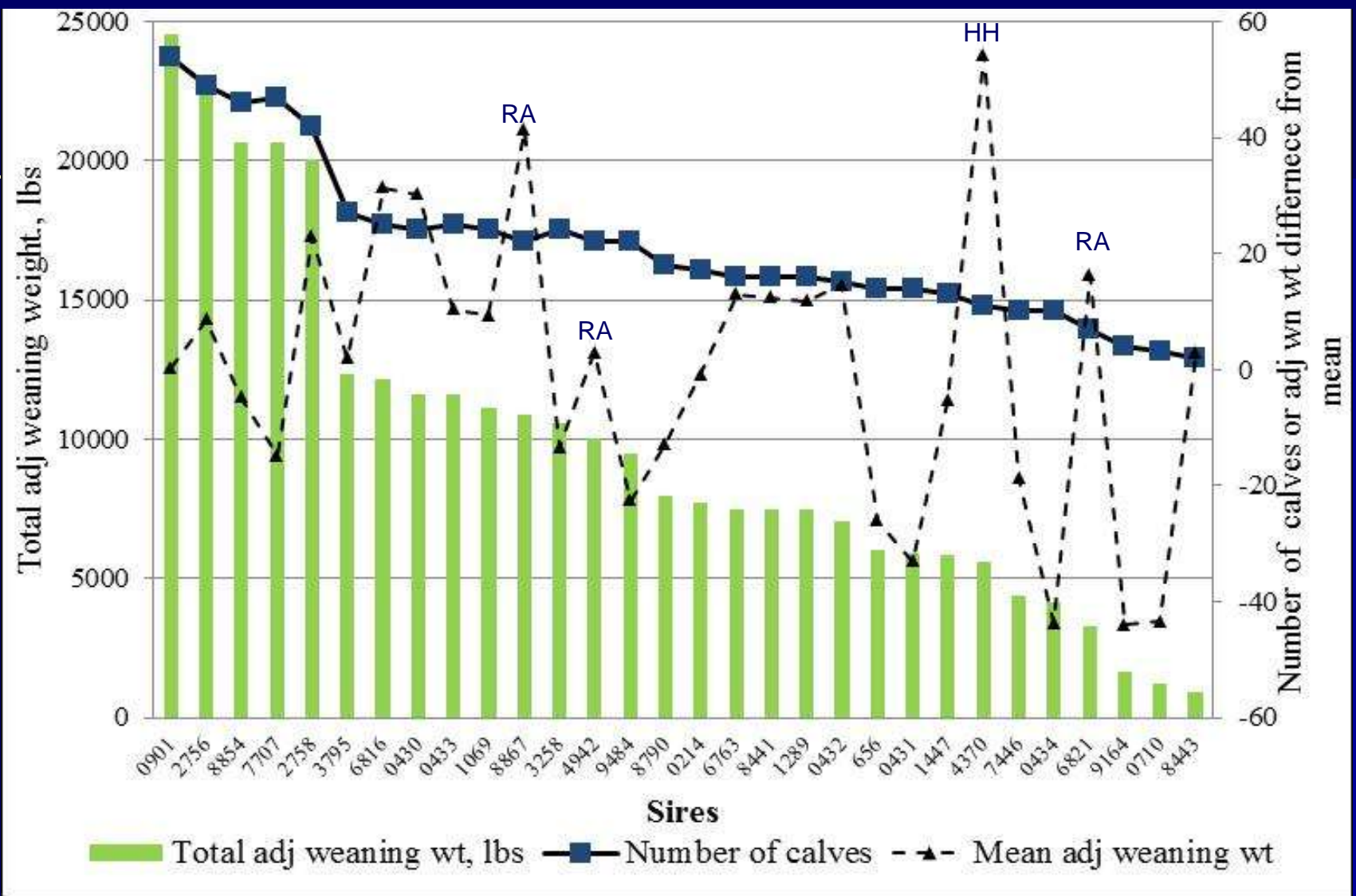
Later (31-60 days)

Early (1-30 days)
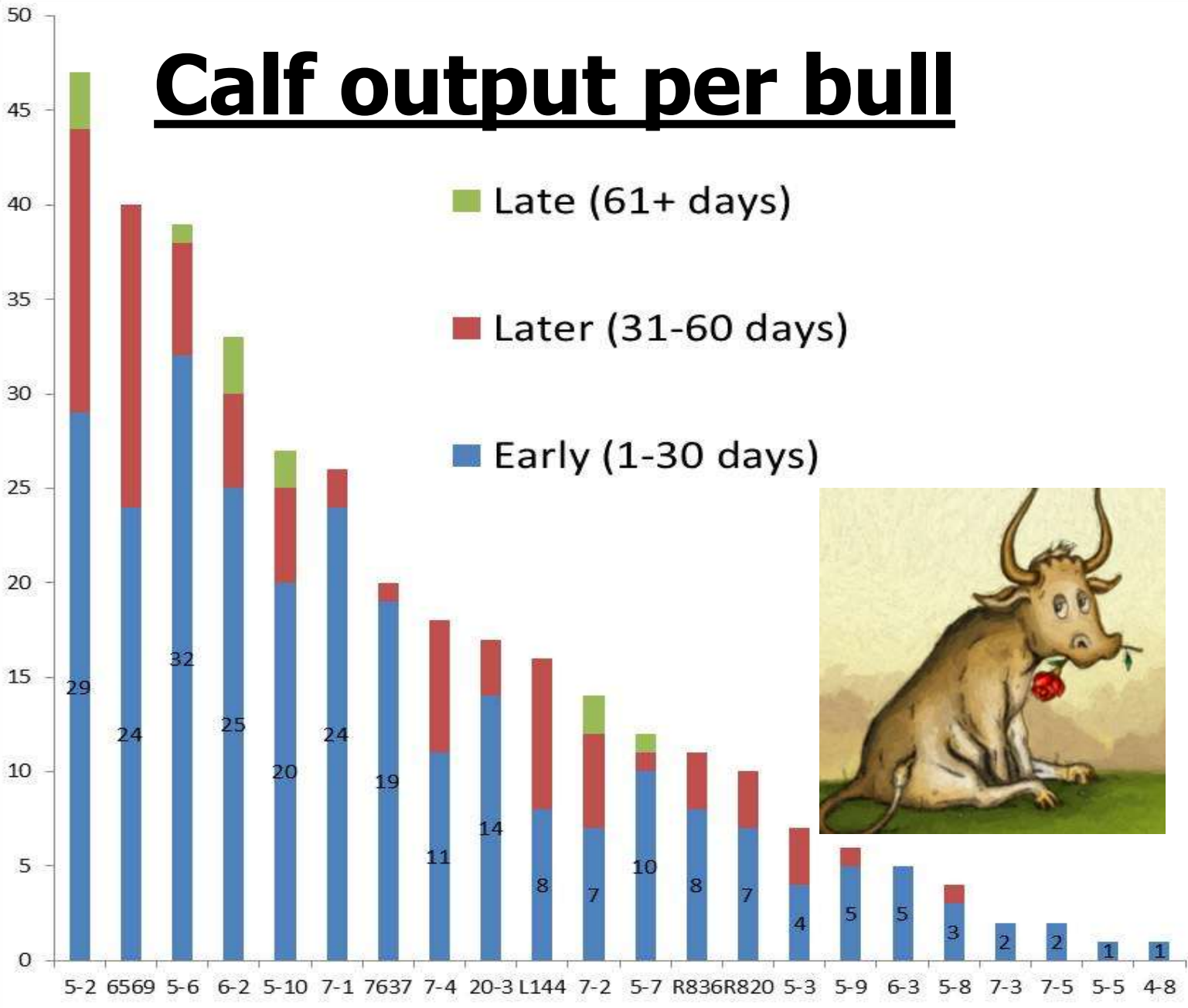
Phenotype of the bulls that sired no offspring

Output of 30 herd bulls total adjusted weaning weight, no. of calves and mean individual calf adjusted weaning weight

D.J. Drake, K.L. Weber, and A.L. Van Eenennaam. 2011. What are herd bulls accomplishing in multiple sire breeding pastures? Proceedings, Applied Reproductive Strategies in Beef Cattle

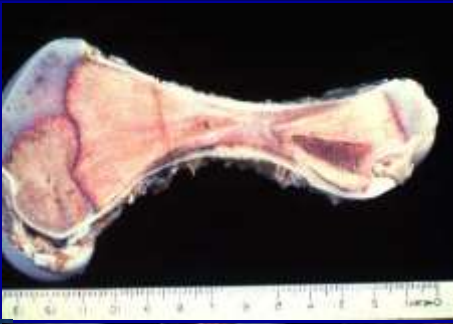# Industry adoption looking at New Zealand as an example

- >200,000 dairy parentage tests out of a herd of about 4.6M cows. ~10% of the commercial tier. Most of these tests are SNP based.

- 20% of the ram, and 30% of the deer breeding industry (majority of stag breeders); mostly microsatellite-based parentage tests

- One of the reasons for the widespread adoption of this technology is the development of an integrated ID and collection system

- This is especially important for lower value animals such as sheep

- If DNA samples are already being collected for parentage verification or as part of a national animal identification scheme, then other DNA technologies can be introduced cost-effectively.

McEwan, J. C. 2007 Current status and future of genomic selection. Proceedings of the New Zealand Society of Animal Production 67: 147-152.; and pers. comm.

Genetic Abnormalities

Images from an article by David S. Buchanan, Department of Animal Sciences, North Dakota State University
http://www.ag.ndsu.edu/williamscountyextension/livestock/genetic-defects-in-cattle

Compare dwarfism response in the 50s to the response to curly calf (AM)

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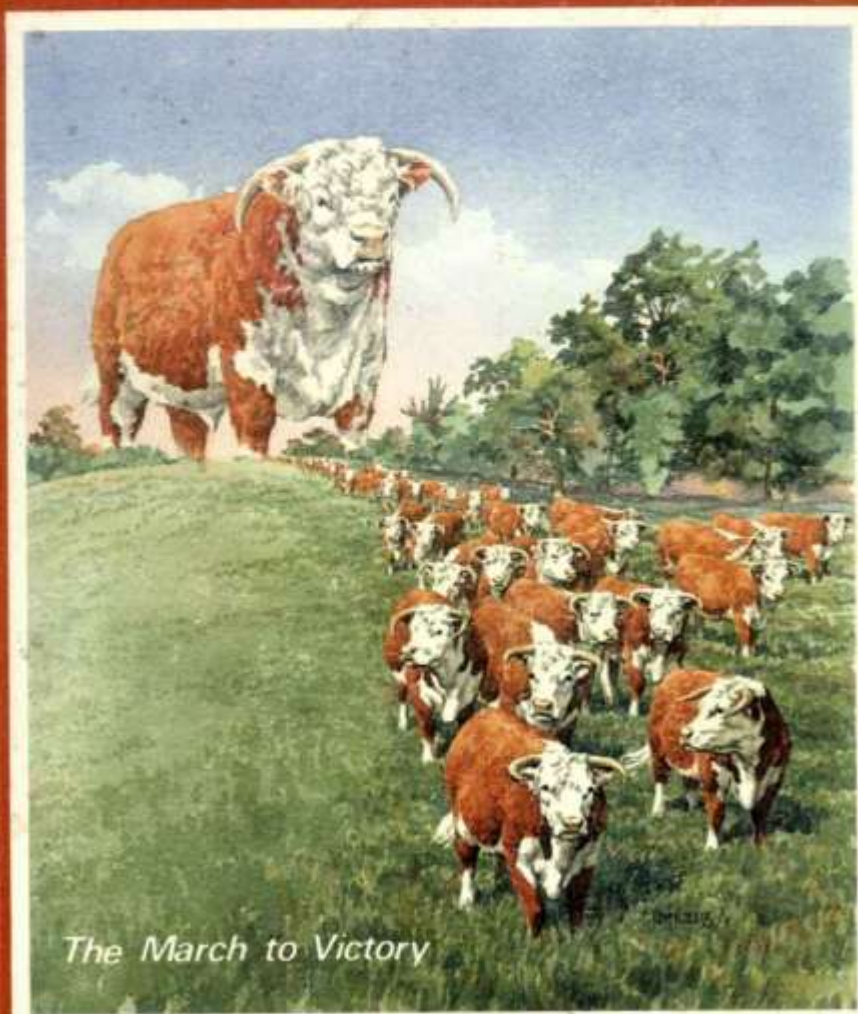
Based upon his height and age, he was less than a frame score 1.

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

THE BATTLE OF BULL RUNTS

By L. P. McCANN

The March to Victory

A 1956 survey of Hereford breeders in the USA identified 50,000 dwarf-producing animals in 47 states. Through detailed pedigree analysis and test crosses, the American Hereford Association, in concert with breeders and scientists, virtually eliminated the problem from the breed. Because carrier status was difficult to prove and required expensive progeny testing, some entire breeding lines were eliminated.

Curly calf – Arthrogryposis multiplex

- From a scientific standpoint, AM is the complete deletion of a segment of DNA that encompasses two different genes

- One of these genes is expressed at a crucial time in the development of nerve and muscle tissue. The mutation results in no protein being produced from this gene and therefore it is unable to carry out its normal function so homozygotes show phenotype

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 of suspect animals shown to be free of AM allele**

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

Other recessive genetic defects with a DNA test

Lethal Congenital Hydrocephalus (NH): Born near term, 25-35 lb birth weights, head is volleyball to basketball sized

Fawn Calf Syndrome (CA): calves at birth assume an abnormal crouched posture, resembling an elk or deer fawn

Why are more genetic defects appearing now?

Naturally-occurring recessive genetic defects are common in all species, and only become evident when certain lines of cattle are used very heavily, such that both cows and bulls have common ancestors in their pedigree, (double bred descendants) thereby allowing a rare genetic defect to become homozygous in their offspring

Estimates of US and Australia genetic testing costs (Angus)

	US	AUSTRALIA
AM (Curly calf)	113,526	12,021
NH	77,067	9,936
CA (Fawn Calf)	28,837	2,532
TOTAL NUMBER	294,054	34,991
COST (@ $25/test)	7,351,350	874,775

Numbers kindly shared by Bryce Schumann, American Angus Association; and Carel Teseling, Angus Australia

Using DNA information for Marker-assisted selection

- Testing for genetic defects e.g. curly calf
- Testing for simple (single gene) traits
- Marker-assisted selection for multigenic or qualitative traits

Simple (qualitative) traits
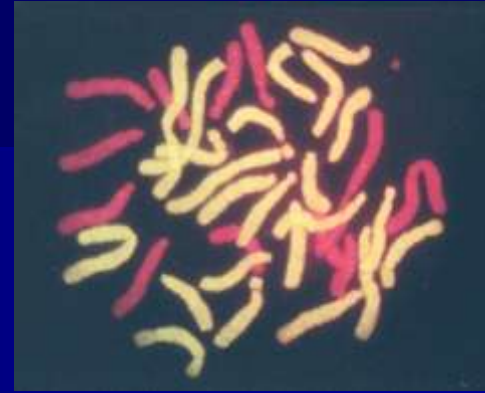
- Genotype = phenotype
  - Gender (male, female)
  - Coat color
  - Double muscling
  - Horns
  - Genetic defects

Complex (quantitative) traits

Genotype

Environment

Phenotype

Tests for quantitative traits – before 2010 10-100 SNPs

- Meat Tenderness
- Quality Grade (Marbling)
- Beef Cattle Feed Efficiency
- Meat Yield
- Dairy Form
- Milk and Milk Component Yield

GeneSTAR®

Which would you rather have???

- A bull that is 'homozygous' for a positive genetic variant with a low-accuracy EBV of +3, or

- Or an unrelated bull carrying no copies of that genetic variant with a low-accuracy EBV of +3

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Both are important!!

- The 'homozygous' bull is a source of favorable form of the genetic variant. Can eventually be used to create homozygous calves

- The other bull contributes other favorable genes, which will improve the other genes affecting the trait.

- Breeding the marker-associated form of the gene into the bull that has no copies should improve the trait by combining all of the good forms of the genes together in one animal

What was wrong with this model of using a few SNPs ?

- A few markers were not sufficient to account for much (>10%) of the genetic variation
- Little genetic progress likely to result from marker-assisted selection
- Markers do not exist for many important traits
- Early adopters of genotyping for marker-assisted selection in livestock have not experienced sufficient value capture i.e. they are too expensive !

A different model: Genomic selection

Alternative is to trace all segments of the genome with markers

- – Divide genome into chromosome segments based on marker intervals?
- – Capture all Quantitative Trait Loci (QTL) all genetic variance
- – Marker density must be sufficiently high to ensure that all QTL are marked by a SNP

Genomic selection is enabled by high-throughput genotyping technology

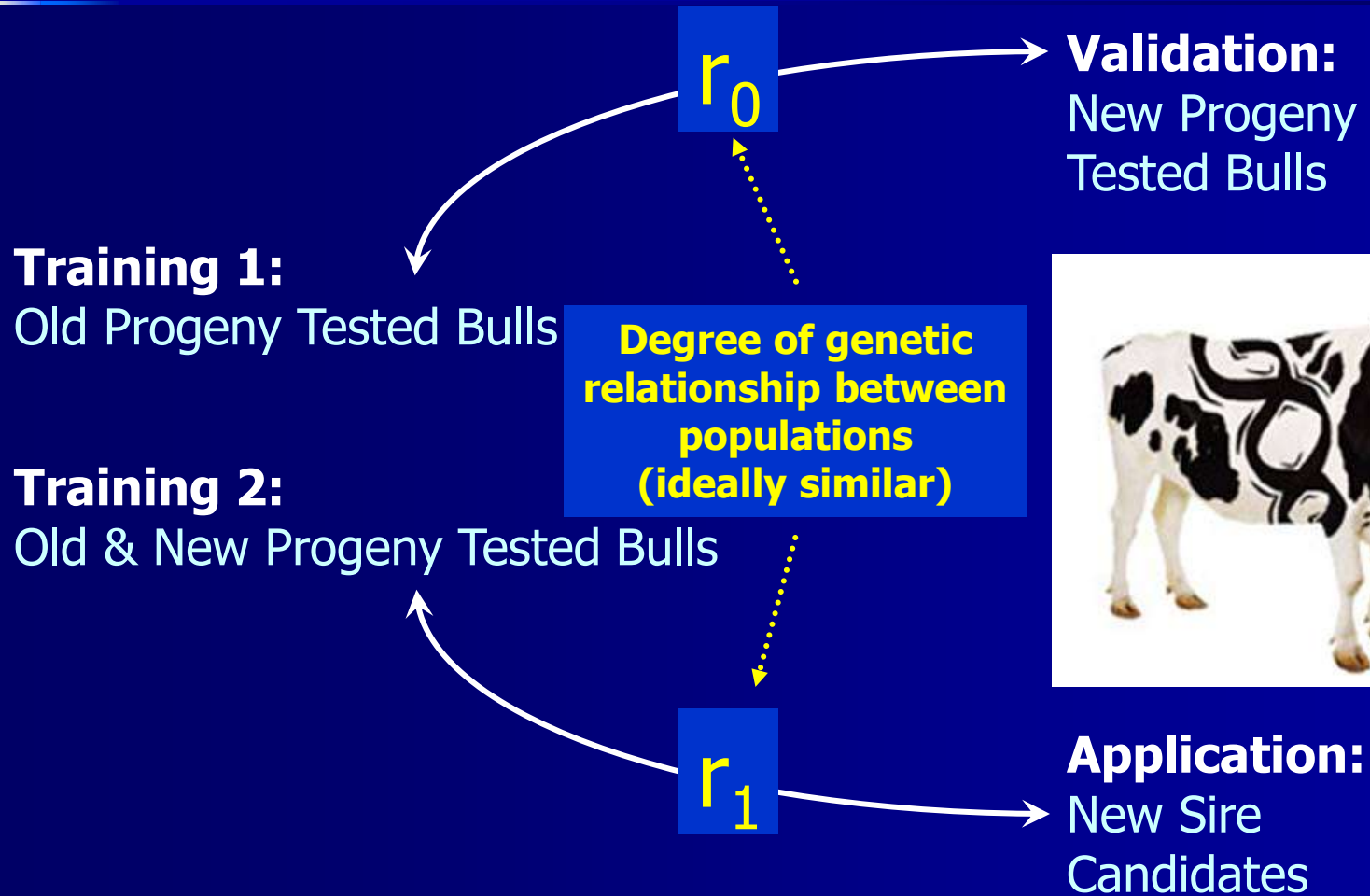- The sequencing of the bovine genome allowed for the development of a 50,000 marker chip!

- Can simultaneously test 50,000 markers

How does Genomic Selection work?

Validation:
New Progeny
Tested Bulls

r_0

Training 1:
Old Progeny Tested Bulls

Degree of genetic relationship between populations (ideally similar)

Training 2:
Old & New Progeny Tested Bulls

r_1

Application:
New Sire
Candidates

Breeding value prediction in Dairy Sires

Young sire Parent Average
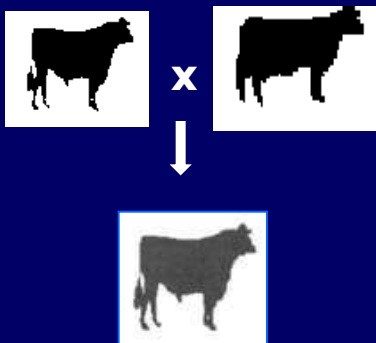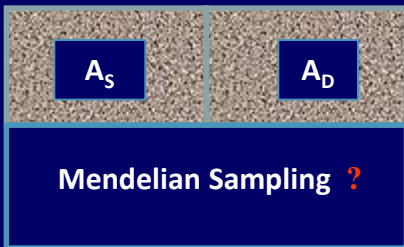
Young sire Progeny Test
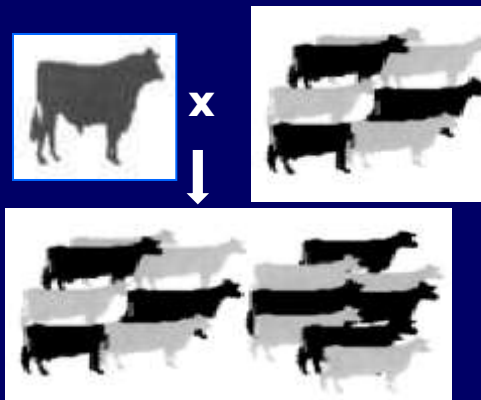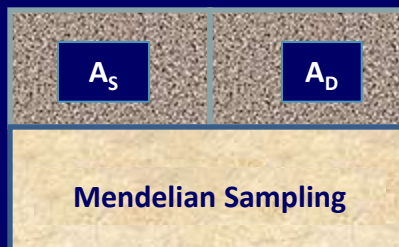
Young sire Genomic Selection

Birth

5 years; >>>> cost

Birth; <<<< cost

A_S A_D

Mendelian Sampling ?

A_S A_D

Mendelian Sampling

A_S A_D

Mendelian Sampling ?
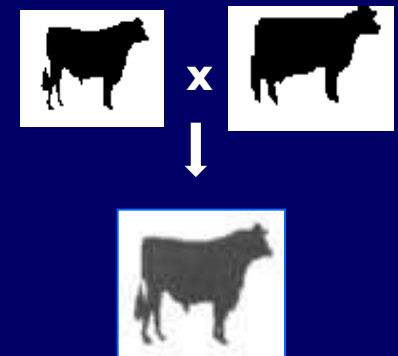
Accuracy 0.20
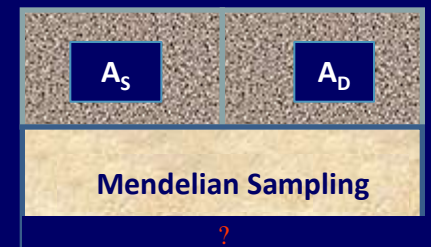
Accuracy 0.80

Accuracy 0.65

Genomic selection objective: Help breeders identify animals with superior breeding values at a young age

$$\Delta G = (\text{intensity of selection } X$$

accuracy of selection X

genetic variation in the population /

generation interval)

Genomic selection could increase rate of genetic gain

Rate of genetic gain ΔG

$\Delta G = (i_m\, r_m + i_f\, r_f)/(L_m + L_f)$ **genetic standard deviation/year**

$= (2*0.8 + 0)/(6+2)$ $= 0.2$ (progeny test)

$= (2*0.6 + 0.8*0.6)/(2+2)$ $= 0.42$ (genomic selection)

$= (2*0.6 + 0.8*0.6)/(.5+.5)$ $= 1.68$ (velogenetics) i.e. 8X

Dairy industry suited to genomic selection

- High use of AI
- Only one breed
- Clear selection goal (total net merit)
- Large number of high accuracy A.I. sires for training
- Extensive, uniform collection of data on traits
- Central evaluation (AIPL) receiving <u>genotypes</u>
- Obvious way to increase rate of genetic gain
- AI companies funding the genotyping because they get a clear cost savings in terms of young sire program

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

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.

Genomic-enhanced Expected Progeny Differences (EPDs) can now be calculated for your animals using the highly predictable American Angus Association database along with IGENITY® profile results to provide a more thorough characterization of economically important traits and improved accuracy on young animals.

Using the IGENITY profile for Angus, breeders receive comprehensive genomic results for multiple, economically important traits.

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
22. Scrotal Circumfrence

ANGUS
THE BUSINESS BREED

Lead Today with 50K

1. Birth weight
2. Weaning weight
3. Weaning maternal (milk)
4. Calving ease direct
5. Calving ease maternal
6. Marbling
7. Backfat thickness
8. Ribeye area
9. Carcass weight
10. Tenderness
11. Postweaning average daily gain
12. Daily feed intake
13. Feed efficiency (net feed intake)

Pfizer Pfizer Animal Health
Animal Genetics

50K SNP chip assays
50,000 SNPs spread
throughout genome

American Angus Association performs weekly evaluations with genomic data

	Igenity	Pfizer
Calving ease (CED)	✓	✓
Growth (BW WW YW Milk)	✓	✓
Residual Average Daily Gain (RADG)	✓	✓
Docility (DOC)	✓	
Carcass (CWT MARB RIB FAT)	✓	✓

http://www.angus.org/AGI/GenomicChoice070811.pdf (updated July 7, 2011)

How much do DNA tests help increase accuracy of EBVs?

	AGI Heritability	AGI HD 50K Correlation	Avg. accuracy (r) for animals with only pedigree estimate and DNA test	Approximate Progeny Equivalents
BW	0.42	0.51	0.71	8
WW	0.20	0.52	0.69	16
YW[2]	0.20	0.64	0.73	20
RADG[3]	0.31	0.65	0.73	13
Milk	0.14	0.32	0.60	12
CW	0.31	0.48	0.63	7
Marb[4]	0.26	0.57	0.70	12
RE[4]	0.32	0.60	0.69	9
FAT[4]	0.26	0.56	0.69	11

[1]These changes are less for higher initial accuracy values
[2]Post-weaning ADG
[3]Dry matter intake
[4]Carcass progeny, not scanned progeny

What is the value of increasing accuracy?

Reg. No.: 12346200
Calved: 5/16/1995
Semen: **$250**
Certificates: $35

Angus Semen Service

Production						Maternal					
CED Acc	BW Acc	WW Acc	YW Acc	YH Acc	SC Acc	CEM Acc	Milk Acc	MkH MkD	MW Acc	MH Acc	$EN
+6 .92	+3.1 .97	+42 .96	+92 .95	+.3 .94	+.07 .94	+9 .90	+18 .94	1378 4501	+84 .89	+.8 .89	-.71

Carcass						$Values					
Cwt Acc	Mrb Acc	RE Acc	Fat Acc	C Grp C Prog	U Grp U Prog	Wean Value	Feedlot Value	Grid Value	QG Value	YG Value	Beef Value
+22 .63	+.22 .67	+.48 .67	+.006 .62	16 35	3465 8164	14.59	34.28	21.71	14.59	7.12	50.7

Fall 2008 EPD

G A R Precision 1680 #11520398

Tehama Bando 155

9J9 G A R 856

Band 234 of Ideal 3163
Tehama Blackcap G373
Rito 9J9 of B156 7T26
Blackbird G A R 833

W C C Blackcap C9 +11911768 R

S S Traveler 6T6

Premier Blackcap 6276A

Q A S Traveler 23-4
S S Miss Power Play 4A4
Brusco
Premier Lady Blackcap 2861U

Reg. No.: 15399709
Calved: 4/1/2006
Semen: **$25**
Certificates: $35

Angus Semen Service

Boyd Heritage was not only Champion sale bull in Denver, he was the high selling bull at $55,000. As Champion of the North American International he displayed flawless structure and confirmation. Heritage stems from the cow family behind bulls like Traveler 004, New Day, On Target, Beef Maker, and Poundmaker. This low 6 frame bull promises excellent growth, thickness, maternal strength and carcass merit. BW 87 lb., WW 744, YW 1,288.

Production						Maternal					
CED Acc	BW Acc	WW Acc	YW Acc	YH Acc	SC Acc	CEM Acc	Milk Acc	MkH MkD	MW Acc	MH Acc	$EN
I +6 .05	I +3.3 .05	I +45 .05	I +83 .05	I +.1 .05	I +.19 .05	I +9 .05	I +32 .05		I +55 .05	I +.7 .05	-7.82

Carcass						$Values					
Cwt Acc	Mrb Acc	RE Acc	Fat Acc	C Grp C Prog	U Grp U Prog	Wean Value	Feedlot Value	Grid Value	QG Value	YG Value	Beef Value
I +15 .05	I +.45 .05	I +.44 .05	I +.015 .05			24.69	24.18	29.86	22.95	6.91	51.99

Fall 2008 EPD

C A Future Direction 5321

G A R Precision 1680

C A Miss Power Fix 308

Tehama Bando 155
9J9 G A R 856
S A F Power Fix
C A Lady Eight 1015

Boyd Forever Lady 7120

A A R New Trend

S V F Forever Lady 57D

V D A R Shoshone 548
Donna A A R 74
Leachman Right Time
S V F Forever Lady 1128

Approx. cost of commercial tests
(estimates only!! - derived from web-sites or personal experience - not official quotes!!)

Test	Species	Cost ($US)
Parentage	Cattle	**$ 13-25**
Genetic Defects	Cattle	**$ 15-150**
3K (just the genotypes)	Cattle	**$ 38**
50K (just the genotypes)	Cattle	**$150**
800K (just the genotypes)	Cattle	**$340**
384 Angus Profile (Igenity US/AGI)	Beef Cattle	**$ 65**
3K (Pfizer US)	Dairy Cattle	**$ 45**
50K (Pfizer US/AGI)	Beef Cattle	**$139**
50K (Holstein Ass.)	Dairy Cattle	**$150**
800K (Holstein Ass.)	Dairy Cattle	**$365**
50K (Pfizer NZ)	Sheep	**$756 (NZ$990)**

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What will the future look like?

"It is perhaps the cumulative value derived from using DNA test information for multiple purposes (traceability, parentage, genetic defects, selection, marker-assisted management, product differentiation), in combination with the rapidly-declining cost of genotyping, that will ultimately push the economics of DNA-based technologies over the tipping point towards more widespread industry adoption"
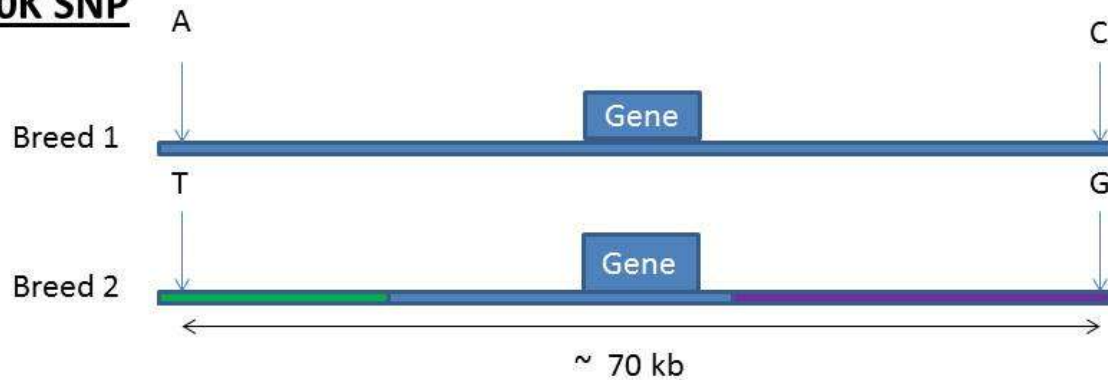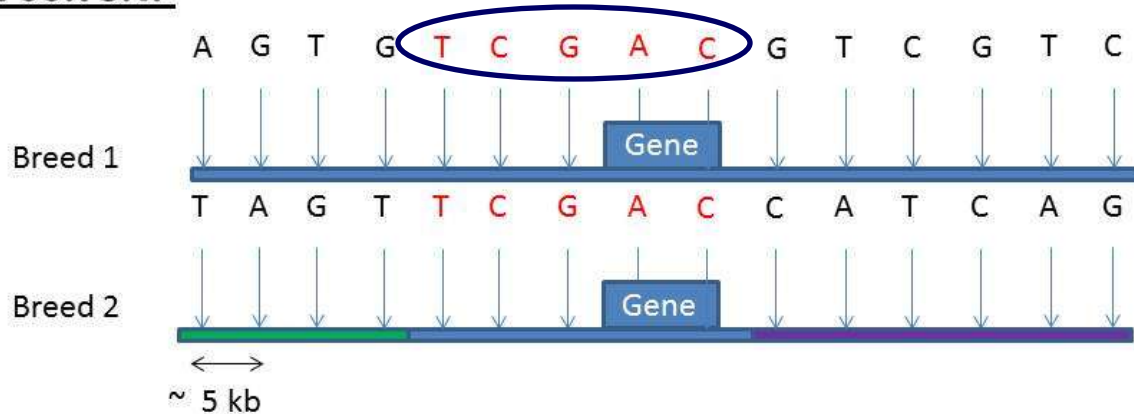
Marker location relative to the gene of interest in two breeds when using the (A) 50K SNP chip assay (markers spaced at ~ 70 kb intervals), or (B) the high density 700 K SNP chip assay (markers spaced at ~ 5 kb intervals)
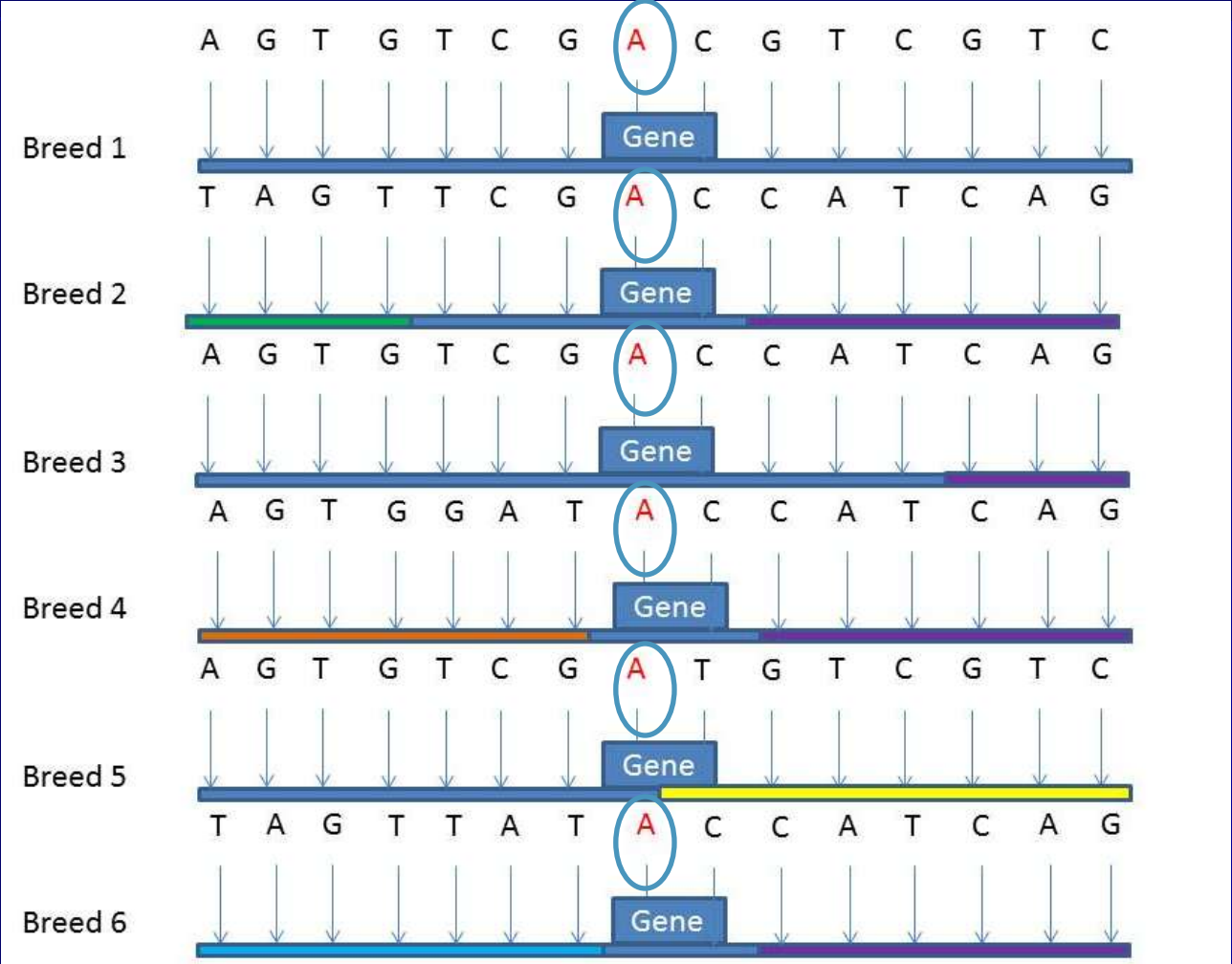
High density panels offer the opportunity to obtain DNA tests that work across breeds

Conclusions

- DNA information has multiple uses

- Parentage and genetic defect testing working well

- Genomic selection working well in dairy cattle

- Starting to get some DNA tests that work in beef – mostly for Angus

- Likely high density chips will help across-breed predictions and help enable DNA tests to work on other beef breeds

- In the future it is hoped that a single DNA test will provide information on parentage, defects, selection, management and mate selection.

This project was supported by 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 Genomics and Biotechnology Education

Questions?

Objective

Estimate the value of using DNA test information to increase the accuracy of beef bull selection in a seedstock breeding program

– The expected returns from using a commercial sire sourced from a seedstock herd using DNA testing

– Additionally, the value of marker information in the selection of replacement stud males to be mated in a seedstock breeding program was also estimated.
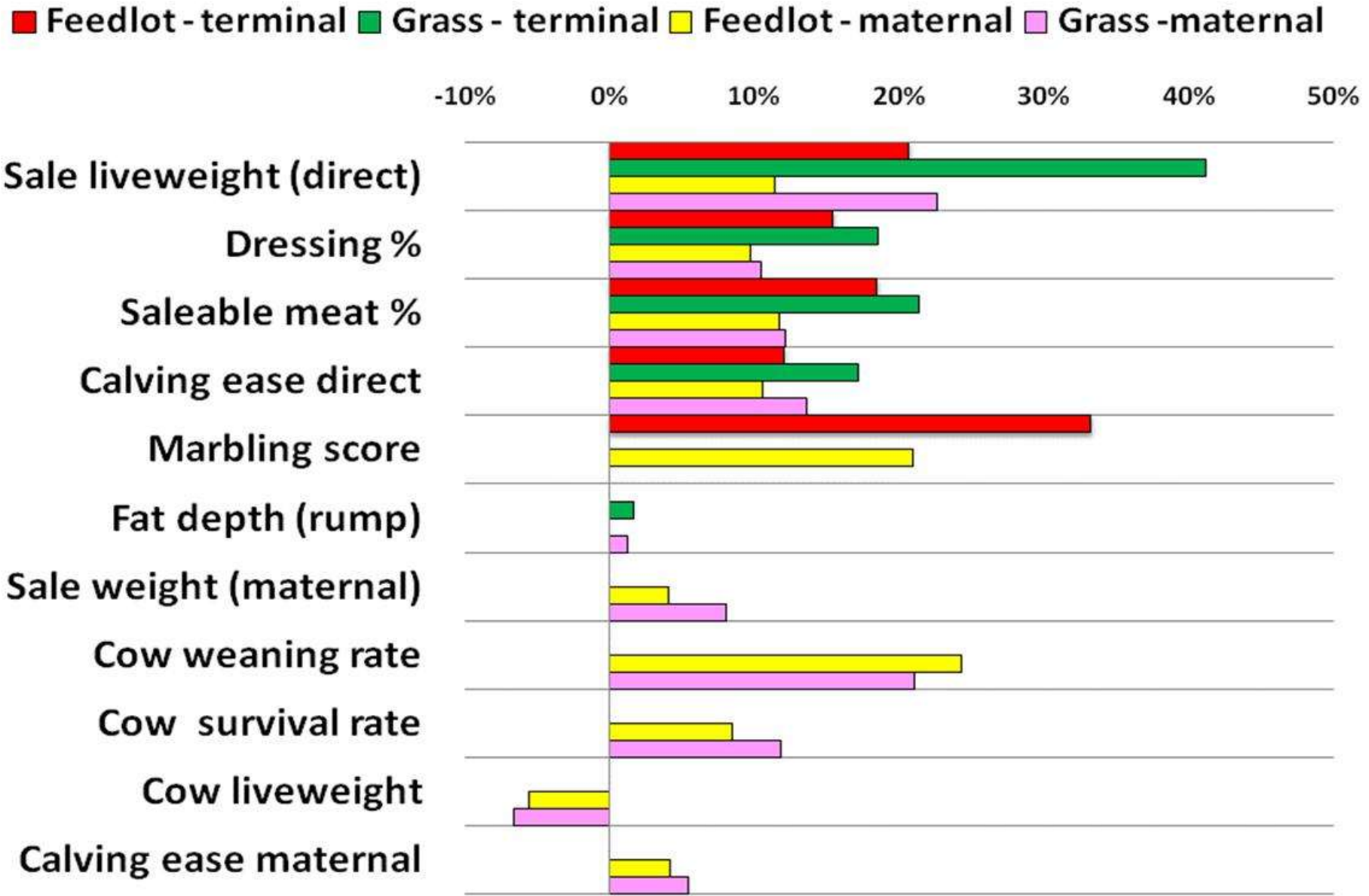
The following seedstock operation was modeled

Parameters	Value
Number of stud cows	600
Number of bulls calves available for sale/selection	267 (all get tested with DNA test)
Number of stud bulls selected each year	8 (~3%; i = 2.27)
Number of bulls sold for breeding (annual)	125 (~50%; i = 0.8)
Maximum age of commercial sire	5 (4 breeding seasons)
Commercial cow:bull ratio	25
Number of commercial females	9225
Planning horizon	20 years
Discount rate for returns	7%
Number of live stud calves available per exposure	0.89
Stud cow:bull ratio	30
Cull for age threshold of cow	10
Age structure of breeding cow herd (2-10 yr)	0.2, 0.18, 0.17,0.15, 0.12, 0.09, 0.05, 0.03, 0.01
Bull survival (annual)	0.8
Age structure of bulls in stud herd (2-4 yr)	0.41, 0.33, 0.26
Age structure of bulls in commercial herd (2-5 yr)	0.34, 0.27, 0.22, 0.17

Legend: Feedlot - terminal (red), Grass - terminal (green), Feedlot - maternal (yellow), Grass - maternal (pink)

Categories: Sale liveweight (direct), Dressing %, Saleable meat %, Calving ease direct, Marbling score, Fat depth (rump), Sale weight (maternal), Cow weaning rate, Cow survival rate, Cow liveweight, Calving ease maternal

High (h²) and intermediate (½ h²) accuracy DNA tests explaining genetic variation in all of the economically-relevant traits in the breeding objective and selection criteria

Objective Trait	h²
Sale liveweight – direct	0.31
Sale liveweight – maternal	0.04
Cow weaning rate	0.05
Cow survival rate	0.03
Cow weight	0.41
Calving ease – direct	0.10
Calving ease – maternal	0.10
Dressing Percentage	0.33
Saleable meat Percentage	0.56
Fat depth (rump)	0.41
Marbling score	0.38

Selection criteria	h²
Birth weight	0.39
200 d Weight	0.18
400 d Weight	0.25
600 d Weight	0.31
Scrotal Size	0.39
Days to Calving	0.07
Mature Cow Weight	0.41
P8 fat	0.41
RIB fat	0.34
Eye Muscle Area	0.26
Intramuscular Fat	0.25

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.

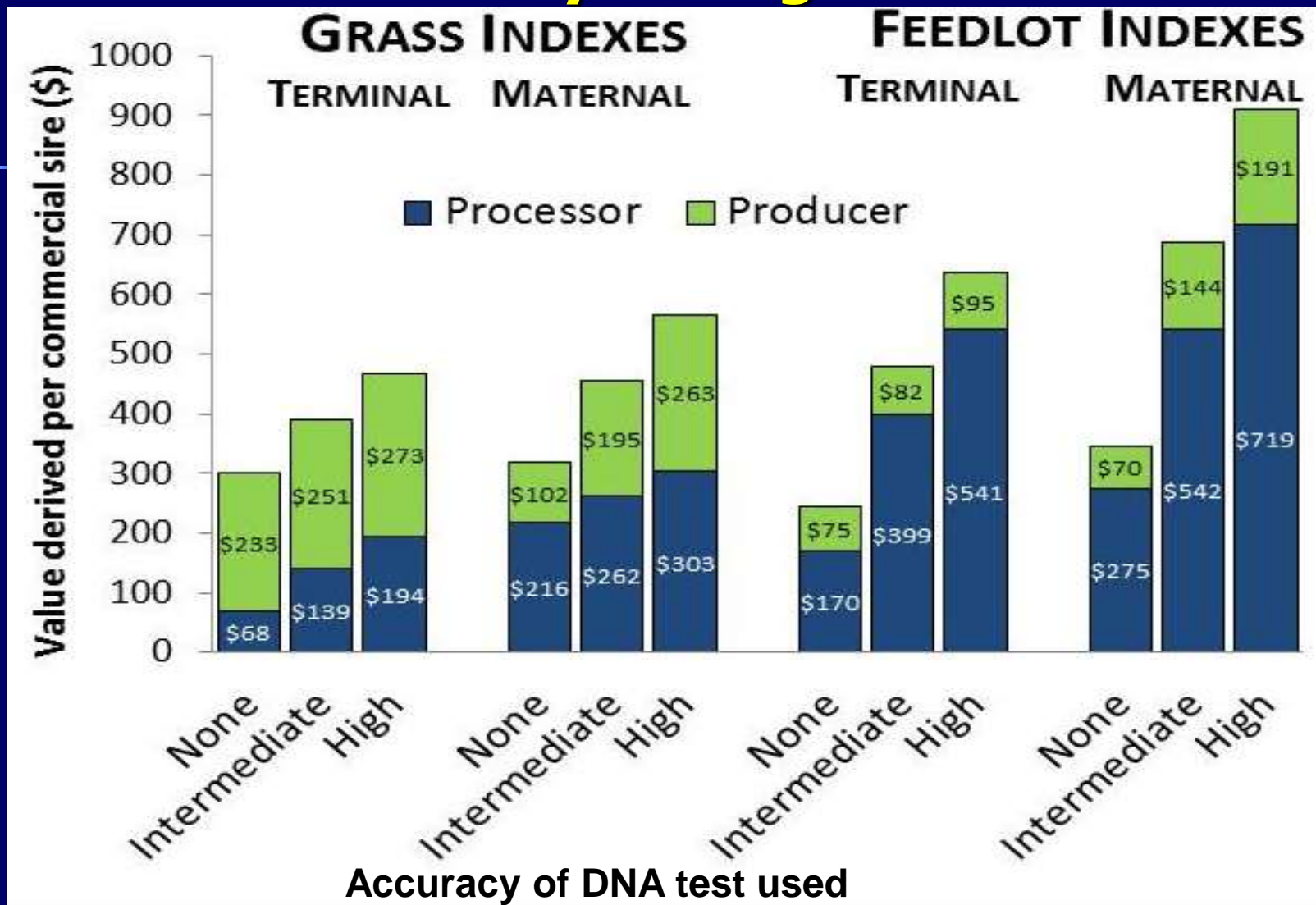# Value of improved selection response for beef seedstock sector due to DNA-test increase in index accuracy

Variable	Unit	Accuracy of DNA test used	GRASS INDEX		FEEDLOT INDEX	
			Terminal	Maternal	Terminal	Maternal
Improvement in selection response	**%**	**Intermediate**	**29**	**46**	**94**	**95**
		High	**54**	**81**	**157**	**158**
Increased value derived from ΔG in commercial sires	$/ DNA test	Intermediate	45	69	118	170
		High	83	124	196	282
Increased value derived from ΔG in stud sires	$/ DNA test	Intermediate	160	203	421	506
		High	297	366	701	836
Total value per test to seedstock operator	**$/ DNA test**	**Intermediate**	**$ 204**	**$ 272**	**$ 539**	**$ 676**
		High	**$ 380**	**$ 490**	**$ 897**	**$1119**

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.

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Industry breakdown of ΔG value derived from increased accuracy from genomic selection

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 (2) *In press.*
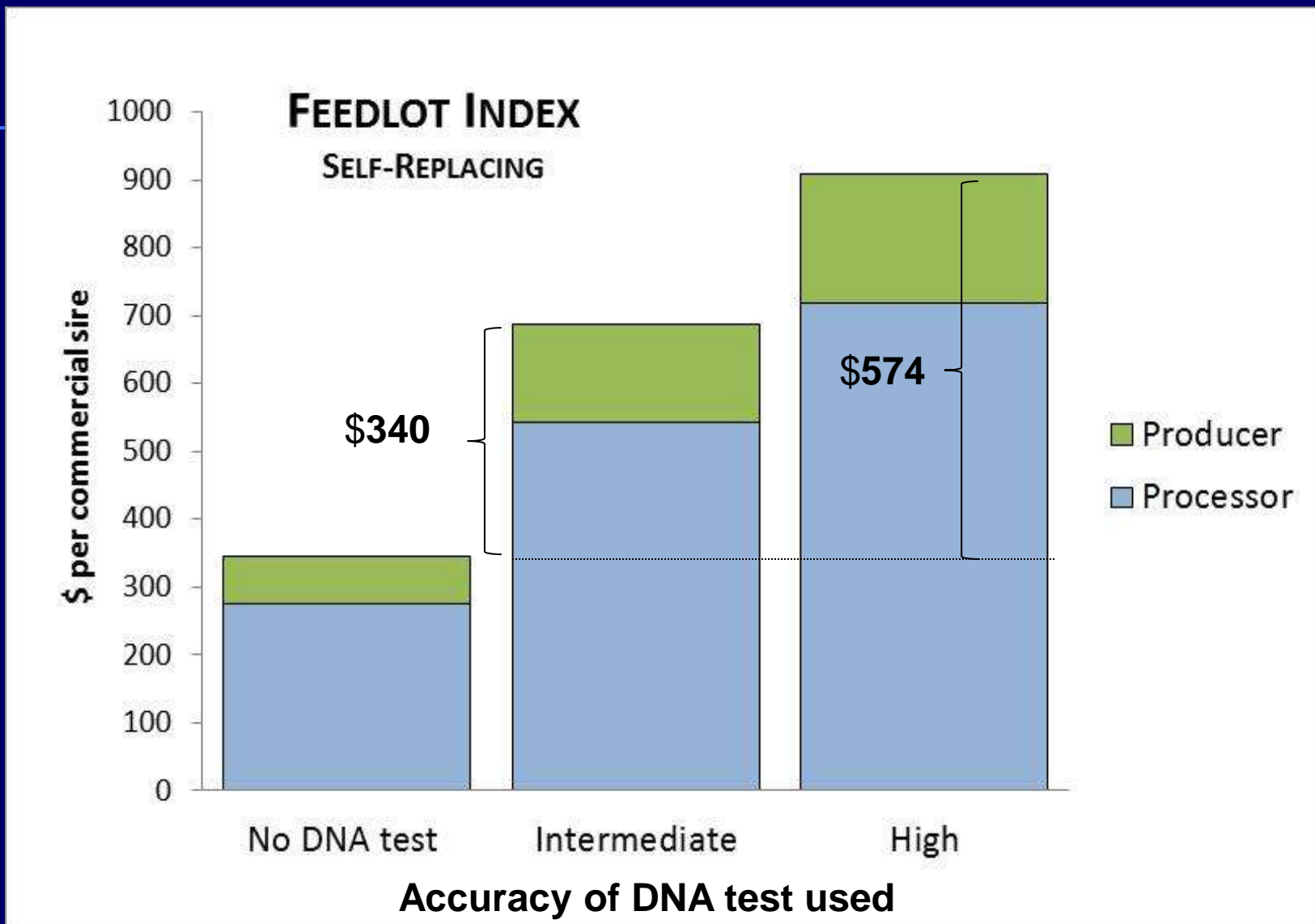
Value of improved selection response for commercial bulls due to DNA-test increase in index accuracy

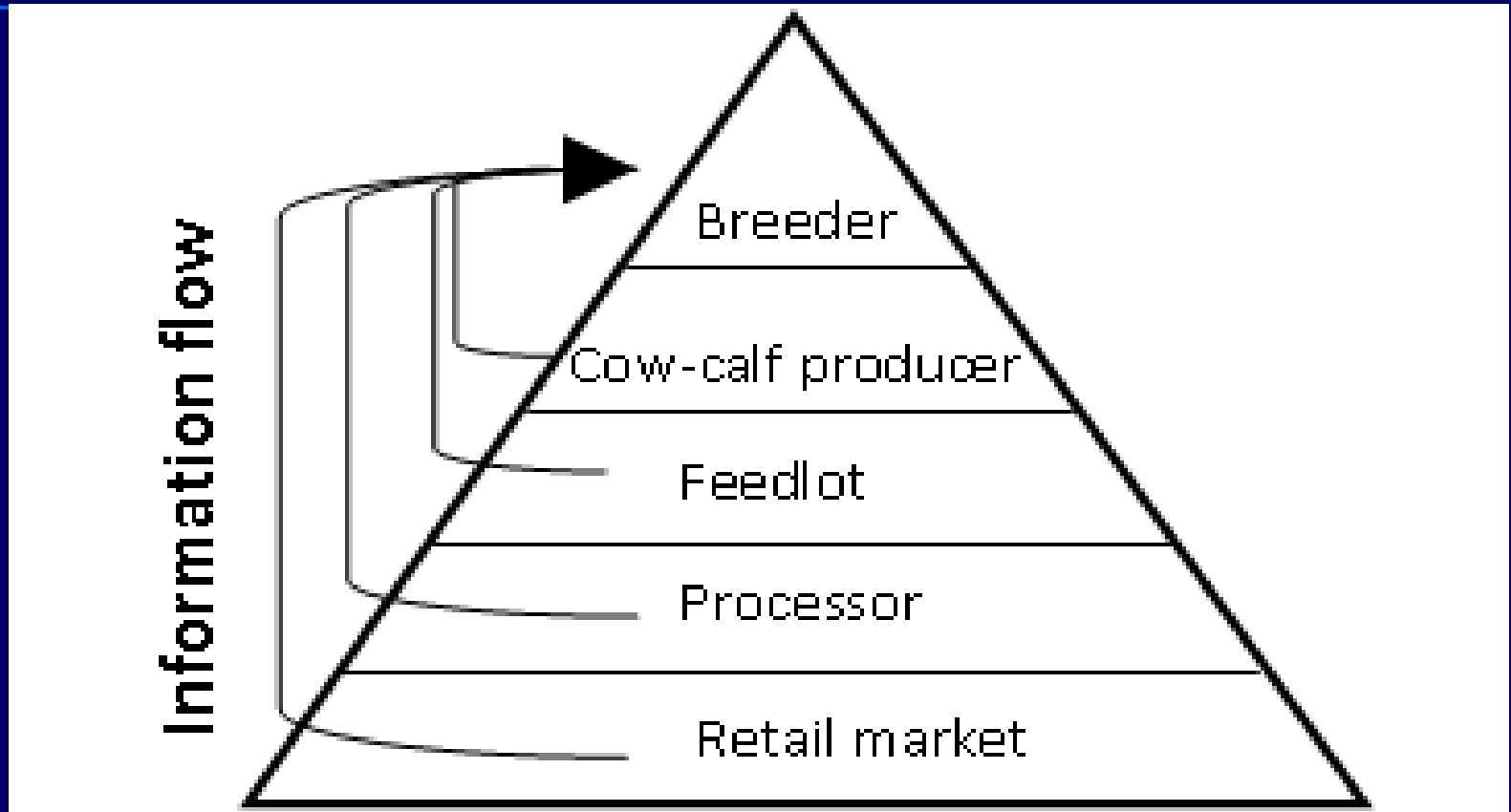| Variable	Unit	Accuracy of DNA test used	Feedlot
Increased value derived from ΔG in commercial sires	**$/ bull**	**Intermediate**	**340**
		High	**574**

Where are returns from genetic gain (ΔG) realized?

The beef industry needs to share data and profit between sectors to most benefit from genomic selection

McEwan, J. C. 2007 Current status and future of genomic selection. Proceedings of the New Zealand Society of Animal Production 67: 147-152.