Where and How in the Beef Cattle Supply Chain Might DNA-based Tests for Disease Generate Value?

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US Bovine Respiratory Disease

Coordinated Agricultural Project

http://www.brdcomplex.org

Bovine Respiratory Disease Complex
Coordinated Agriculture Project

The “Integrated Program for Reducing Bovine Respiratory Disease Complex (BRDC) in Beef and Dairy Cattle” Coordinated Agricultural Project is supported by Agriculture and Food Research Initiative Competitive Grant no. 2011-68004-30367 from the USDA National Institute of Food and Agriculture.

Overview

- Which traits are likely to benefit from genomics?
- What is the value of emerging molecular breeding values (MBV) for economically-relevant traits (ERT) for which no breed EPD exist?
- Calculating relative economic value of BRD as a case study of how this might work
- Other economically-relevant (ERTs) traits
- Industry structure implications
- How might this all work?

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

Rate of change towards breeding objective

$$\Delta G \infty \frac{\textit{accuracy of selection}}{\textit{generation interval}}$$

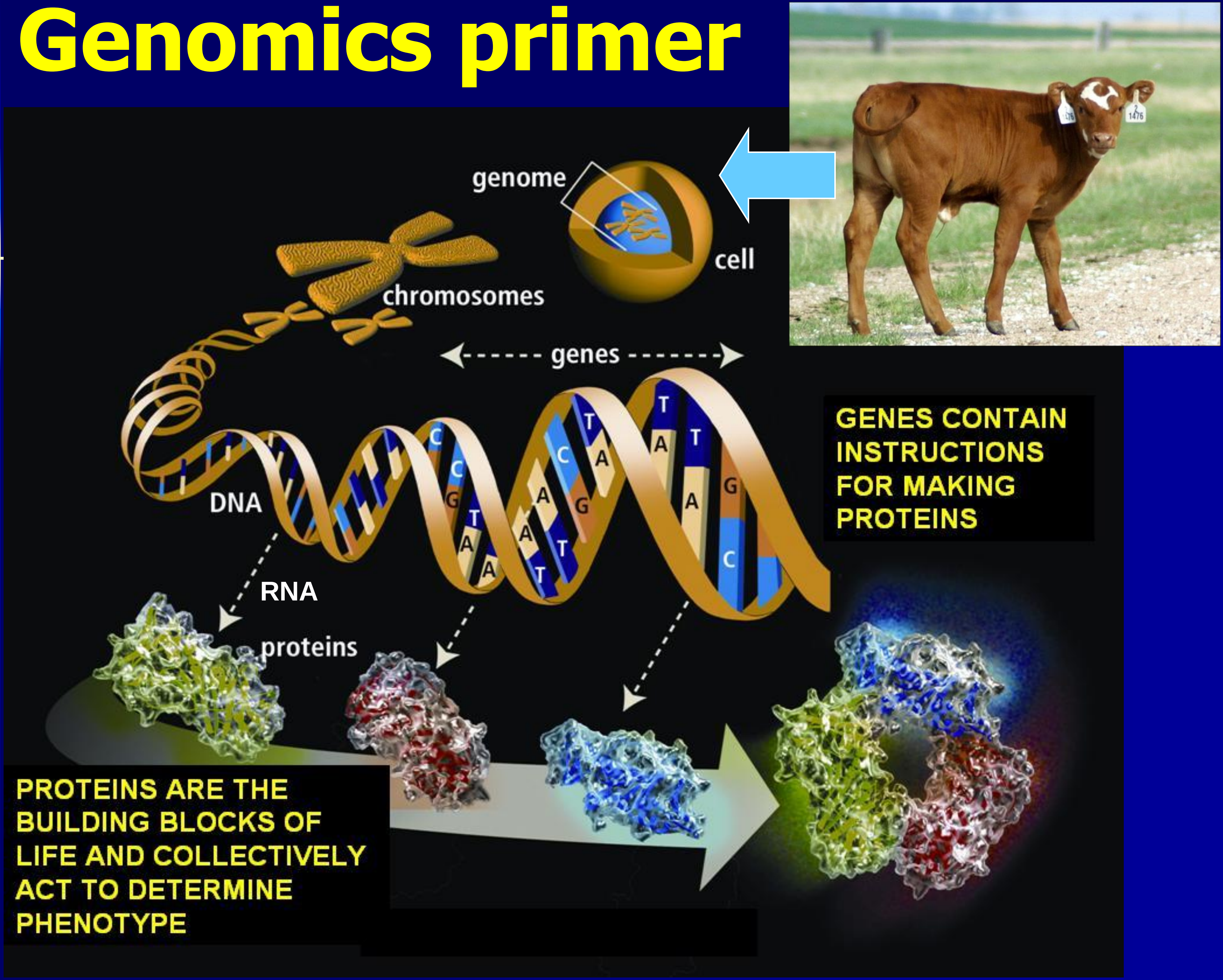
Potential benefits of genomics are greatest for economically-important traits that

- Are difficult or expensive to measure
- Cannot be measured until late in life or after the animal is dead
- Are not currently selected for because they are not routinely measured
- Have low heritability
- Have undesired correlations with other economic traits

Yep, looks like all of them were susceptible

AABP 9/21/2012

Genomics primer

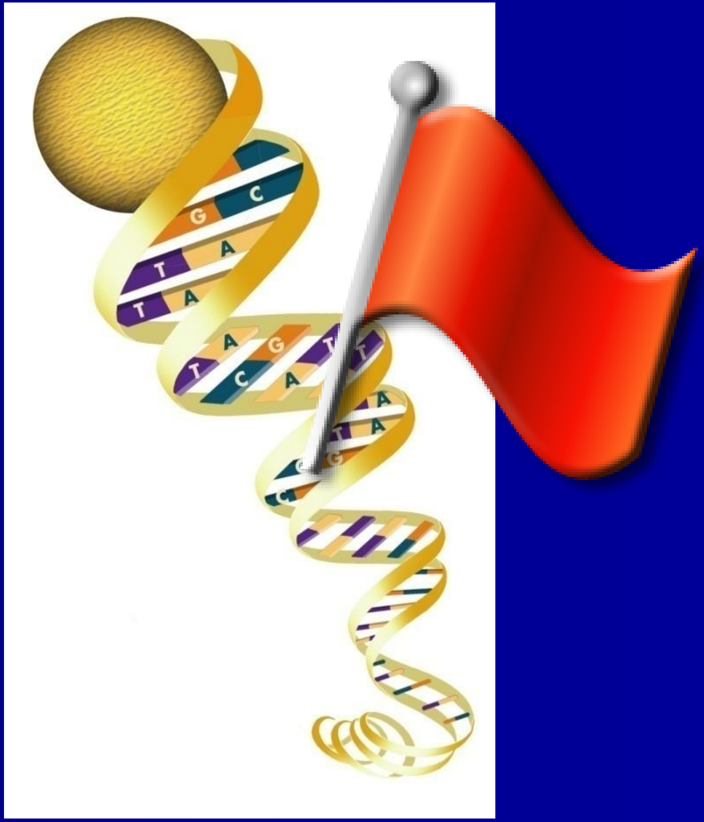


GENES CONTAIN INSTRUCTIONS FOR MAKING PROTEINS

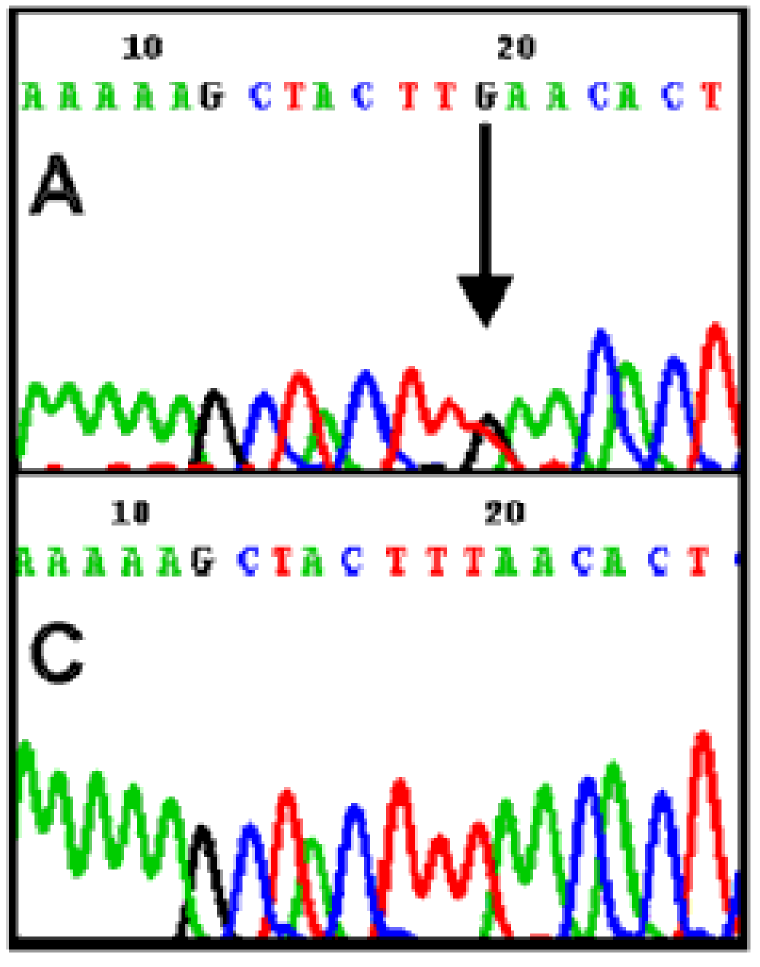
PROTEINS ARE THE BUILDING BLOCKS OF LIFE AND COLLECTIVELY ACT TO DETERMINE PHENOTYPE

SNP (Single Nucleotide Polymorphism)

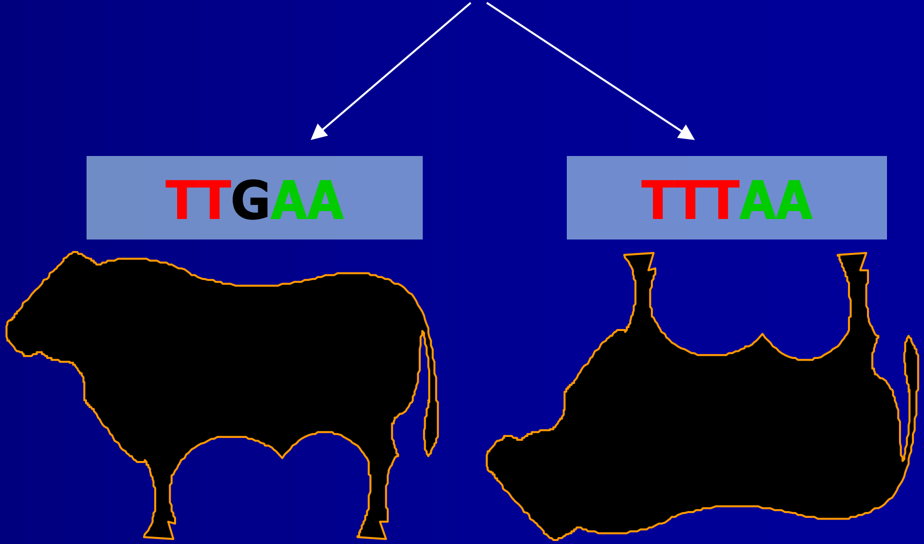
A DNA sequence variation that varies sufficiently between individuals that its inheritance can be tracked through families



Genotyping identifies genetic variation (SNPs)



Heterozygous bull



High-throughput genotyping technology enabled a new approach

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

What is needed for "genomic" selection?

THEORY

- Population
- 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 predict the merit of new animals, not contained in the training data set

Implementation of Genomic Selection in the Dairy Industry

Training 1:
Old Progeny Tested Bulls

Calibration (Validation) (Estimation of r_g):
New Progeny of Tested Bulls

Retraining each generation:
Old Bulls & New Progeny of Tested Bulls

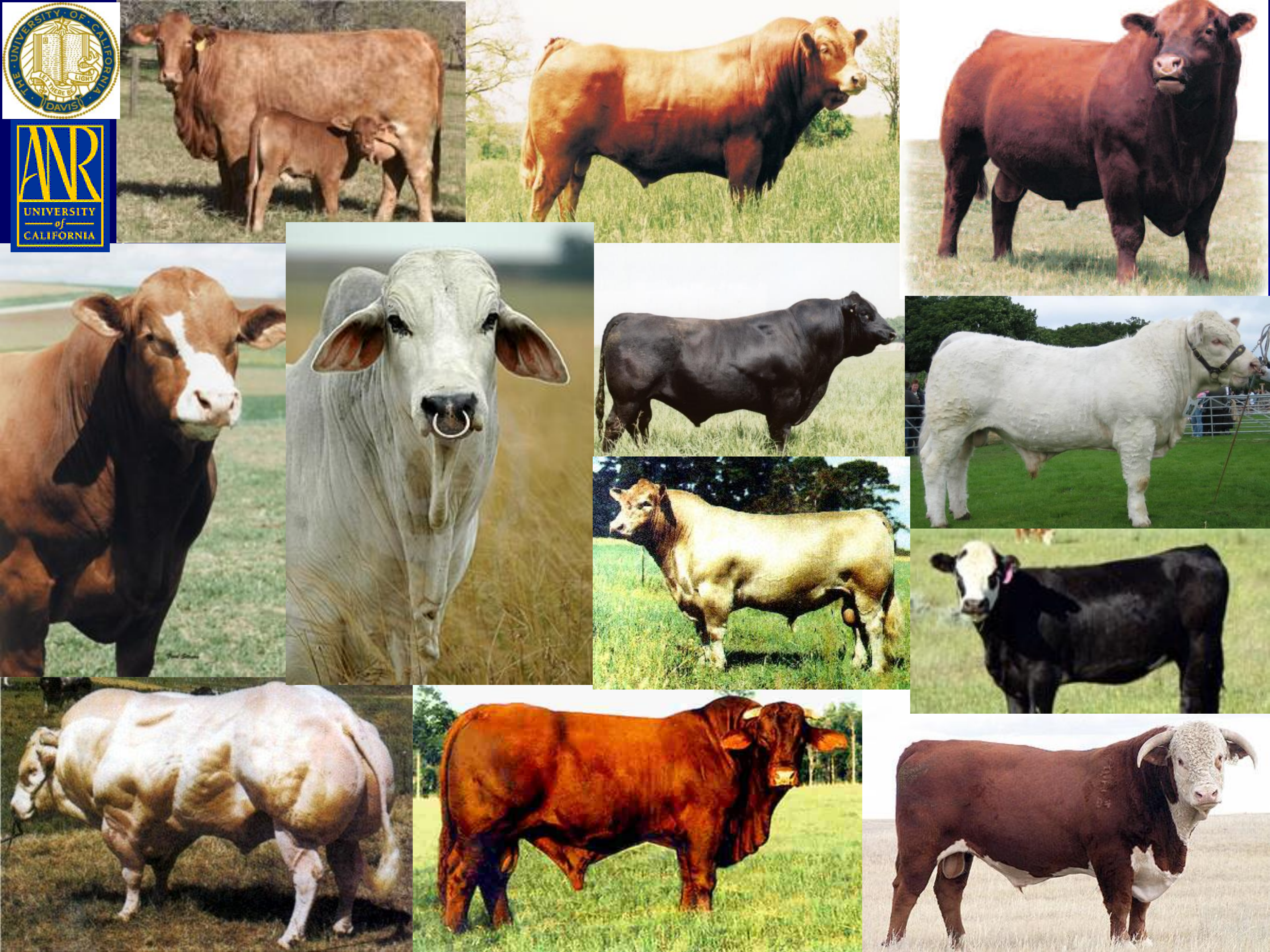
Application:
New Sire Candidates

THE UNIVERSITY OF CALIFORNIA DAVIS

LET THERE BE LIGHT

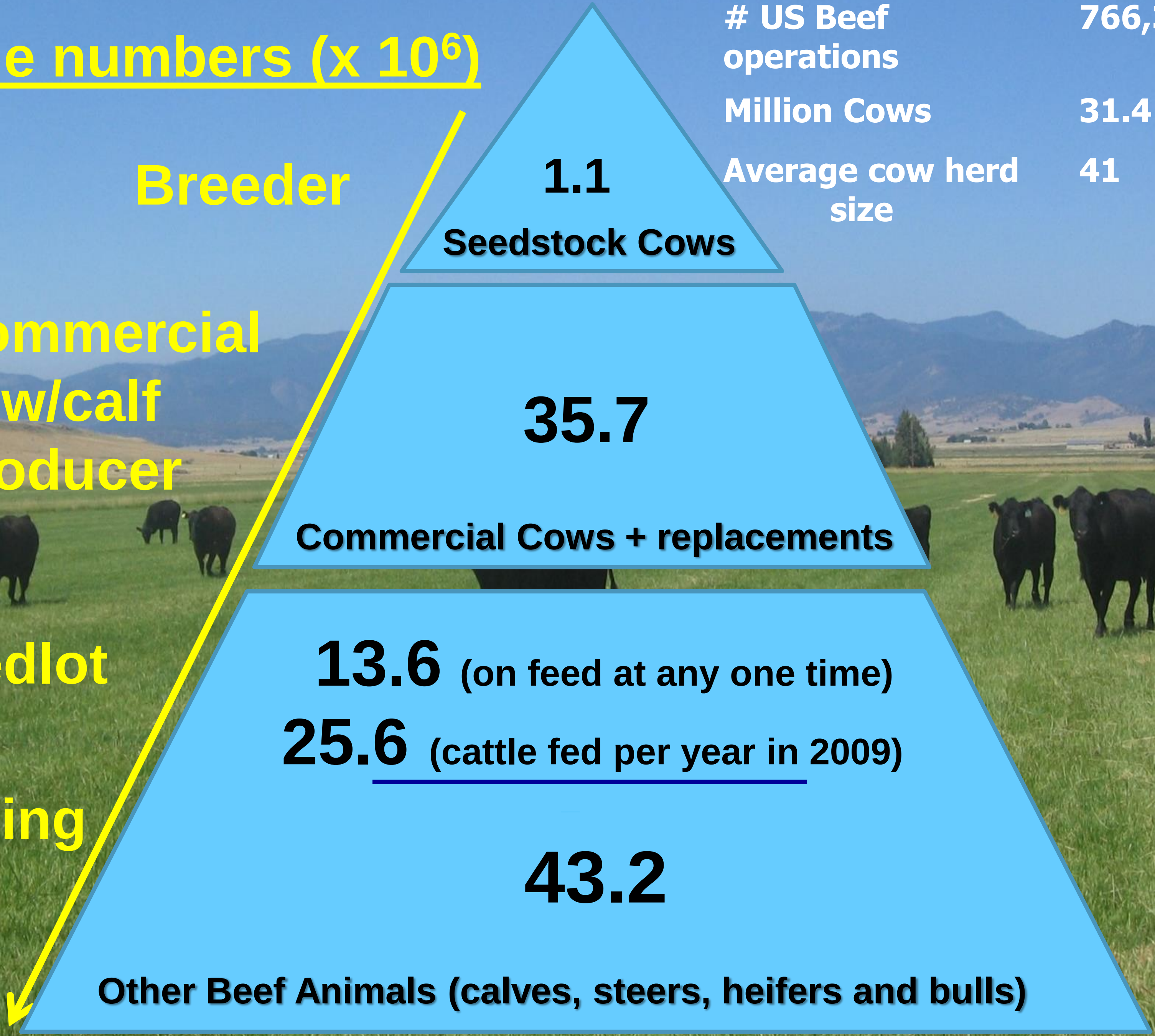
ANR

UNIVERSITY of CALIFORNIA



US cattle numbers (x 10^6)

# US Beef operations	766,350
Million Cows	31.4
Average cow herd size	41



Breeder

1.1

Seedstock Cows

Commercial cow/calf producer

35.7

Commercial Cows + replacements

Feedlot

13.6 (on feed at any one time)

25.6 (cattle fed per year in 2009)

Processing

43.2

Other Beef Animals (calves, steers, heifers and bulls)

Retailer

Genomics may increase the value of genetic gain (ΔG) appreciably if it enables:

1. Selection for economically-relevant traits (ERTs) that were previously omitted from breeding objectives due to lack of selection tools/criteria e.g. disease, feed efficiency, fertility
2. The introduction of novel traits into the breeding objective, or
3. The development of high-value markets with new product specifications.

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What is needed to develop DNA-tests for selection against disease

Large training/discovery populations with BRD case:control (BRD:healthy) and SNP genotypes used to estimate the value of every chromosome fragment contributing variation to BRD susceptibility. This allows for prediction of which chromosome segments or regions are important to confer resistance/susceptibility.

Prediction equation = the results of training can then be used to predict the genetic merit of new animals not contained in the training data set based on their genotype alone.

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Genomic development: High Density SNP Chip

- The ready availability of dense single nucleotide polymorphism arrays (i.e. SNP chips) has given rise to hitherto unforeseen opportunities to dissect between-host variation and identify possible genes contributing to this variation using genome wide association studies (GWAS)

Bishop, S. C., and J. A. Woolliams. 2010. On the genetic interpretation of disease data. Plos One 5: e8940.

770,000 SNPs evenly distributed throughout the genome

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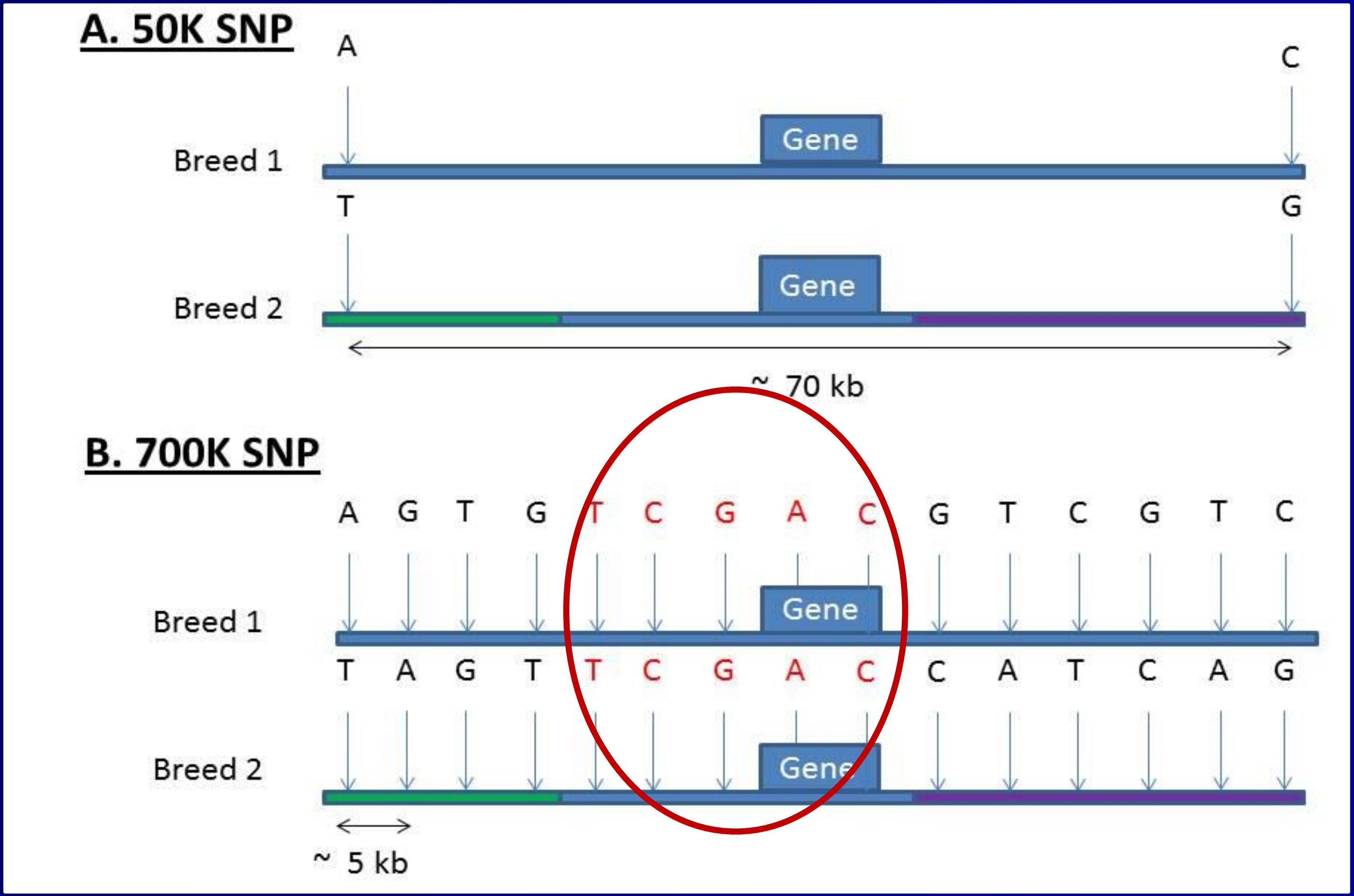
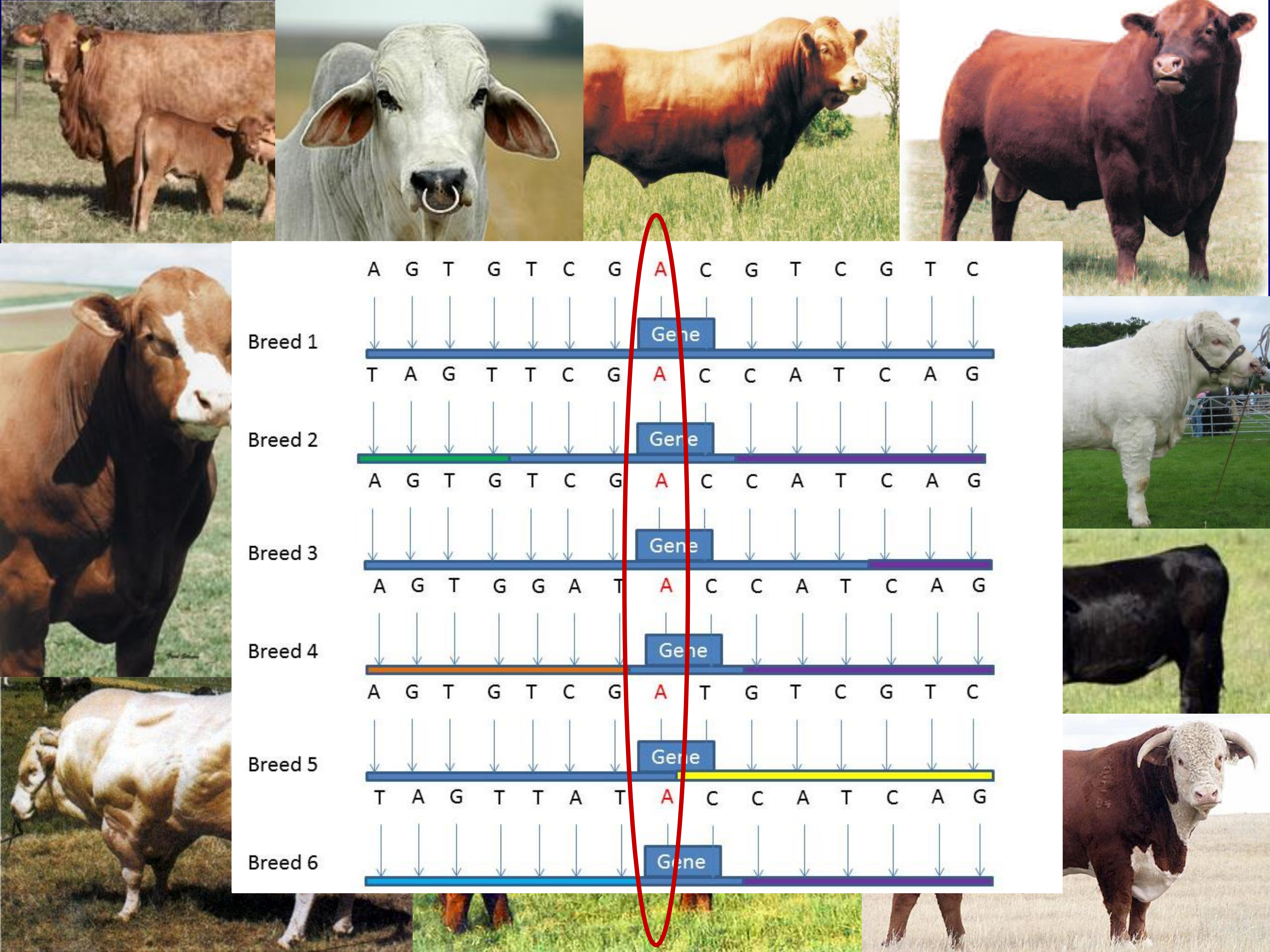
High density SNP chips may enable DNA tests to be predictive across breeds





A G T G T C G A C G T C G T C

Breed 1

T A G T T C G A C C A T C A G

Breed 2

A G T G T C G A C C A T C A G

Breed 3

A G T G G A T A C C A T C A G

Breed 4

A G T G T C G A T G T C G T C

Breed 5

T A G T T A T A C C A T C A G

Breed 6

Determining the value of genomics

- Genomic information should not require any fundamental changes to the development of breeding objectives and selection index calculation
- Selection emphasis for new genomically-enabled traits will need to be weighted by effect on profitability relative to other economically-important traits
- What is the relative economic value of these new traits in the breeding objective?

The Potential Value of DNA-based Tests for Bovine Respiratory Disease (BRD) Resistance to the Beef Cattle Supply Chain

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Objective

To calculate the weighting (i.e. relative economic value) that should be given to selection for BRD resistance in a multi-trait selection index for Angus terminal sires.

Scenario

- A 1000–cow-calf enterprise and retained ownership was assumed
- All progeny of terminal sires were harvested and so no economic value was associated with maternal traits
- Only phenotypes for weaning weight, feedlot average daily gain, feed intake, USDA yield grade, marbling score and BRD incidence (%) contributed to the breeding objective.
- The feedlot phase was divided into three periods. The first period (backgrounding) was terminated at a weight-constant end point of 850 lb. The second (growing) and third (finishing) periods were of 50 and 100 days duration, respectively.

Assumptions

- BRD occurred when calves were moved to the feedlot phase at weaning – incidence rate of 10%
- the fixed cost of feedlot phase was unchanged
- a dead calf incurred no feed costs
- there was a 10% mortality from BRD
- there was a 13% reduction in ADG (1.3 lbs/d) for the first phase of feeding (weaning to 850 lbs)
- final yield grade was reduced by 0.1
- the cost to diagnose and treat a BRD calf was $44

Prices, premiums and discounts used in developing the multi-trait selection index for Angus terminal sires.

Weaned calf weight (lb)	**$/lb**		**$/100lb**
< 350	1.21	Prime	28.07
351-400	1.15	High Choice	5.53
401-450	1.09	Choice	0
451-500	1.04	Select	-10.20
501-550	1.01	Standard	-20.20
551-600	0.96		
>600	0.92	Yield Grade 1	3.00
Carcass weight (lb)	$/100 lb	Yield Grade 2	2.00
Base price	155.95	Yield Grade 3	0.00
<550	-15	Quality/Yield Grade	-10.20
>950	-15	Yield Grade 5	-20.20

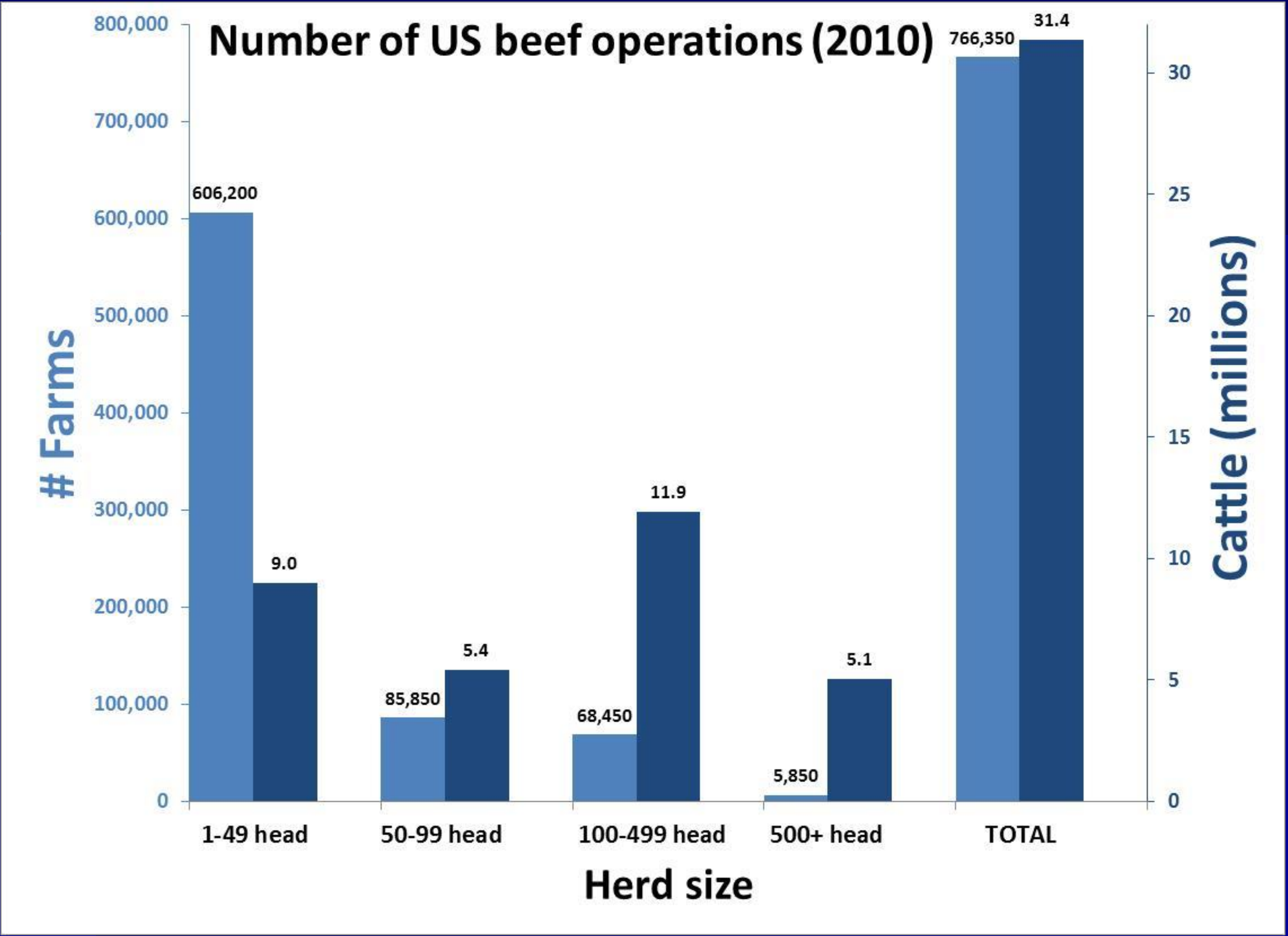
Results: Reducing BRD incidence should get ~6X economic weighting given to growth traits (weaning weight)

Trait (unit)	Economic Value ($)	Genetic SD	Relative economic value (REV)	Relative importance (relative to YG)
BRD incidence (%)	-8424.7	7.94	-66892	**37.7**
Weaning wt. (lb)	241.4	41.76	10081	**5.7**
Feed Intake (lb/d)	-5811.8	1.41	-8195	**4.6**
Feedlot ADG (lb/d)	27654.5	0.24	6637	**3.7**
Marbling score	8926.0	0.51	4552	**2.6**
Yield Grade	-5379.2	0.33	-1775	**1**

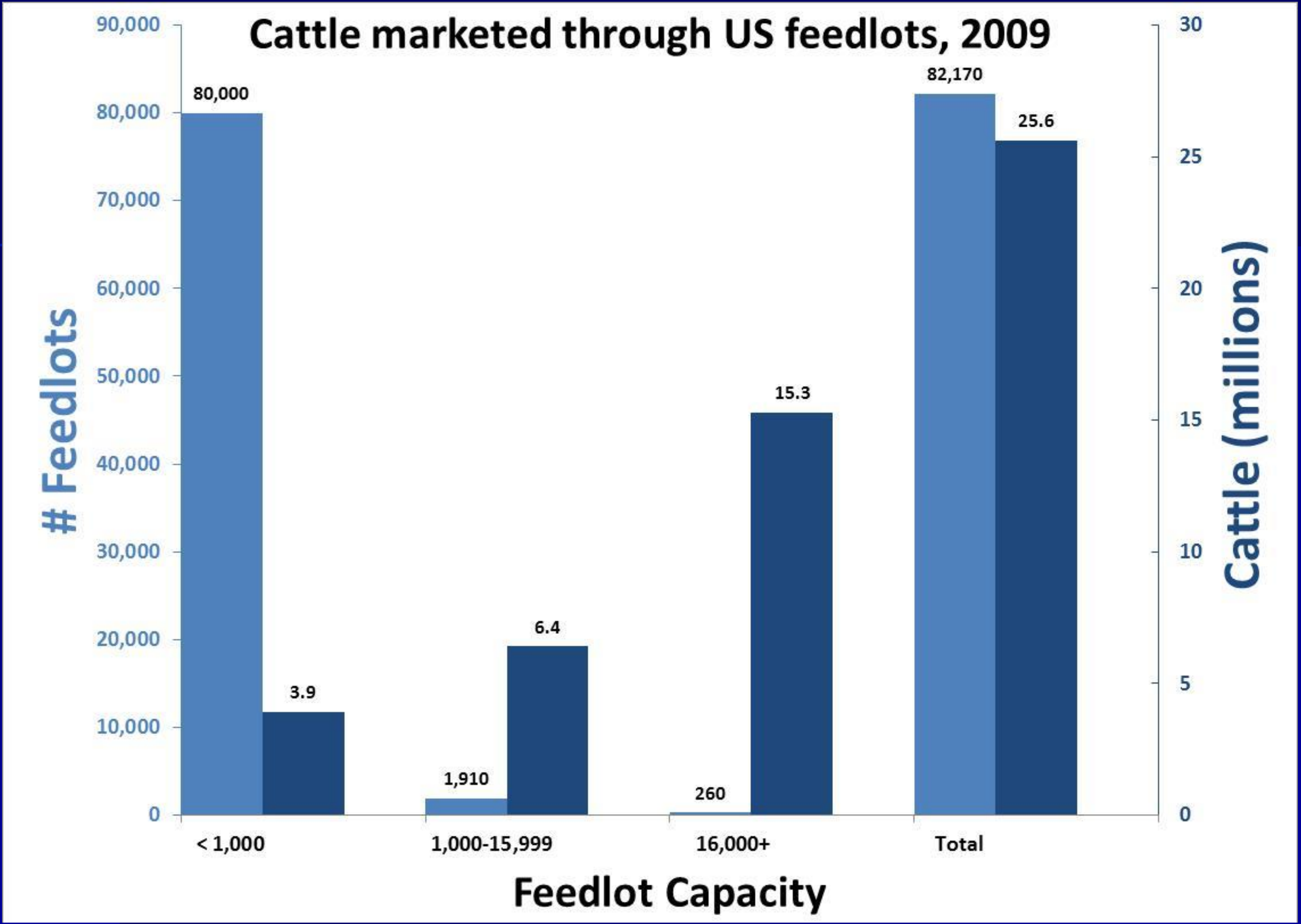
Ninety percent of US cattle operations have fewer than 100 head, and most sell their cattle at auction prior to feedlot entry

This relative economic value scenario was developed to maximize the profitability of a vertically-integrated (retained ownership) production system

- In reality most producers' financial returns are tied very closely to the number of calves, a function of reproduction, and less to feedlot performance and carcass traits, and even less to bovine respiratory disease incidence.
- To incentivize the inclusion of BRD resistance in selection decisions, a mechanism analogous to a calf preconditioning bonus would be needed to equitably share some of the value derived from reduced feedlot disease incidence and to compensate breeders and producers for reducing selection emphasis on other economically-relevant traits.


Number of US beef operations (2010)
Farms
Cattle (millions)
800,000
700,000
600,000
500,000
400,000
300,000
200,000
100,000
0
30
25
20
15
10
5
0
606,200
9.0
85,850
5.4
68,450
11.9
5,850
5.1
766,350
31.4
1-49 head
50-99 head
100-499 head
500+ head
TOTAL
Herd size

Cattle marketed through US feedlots, 2009



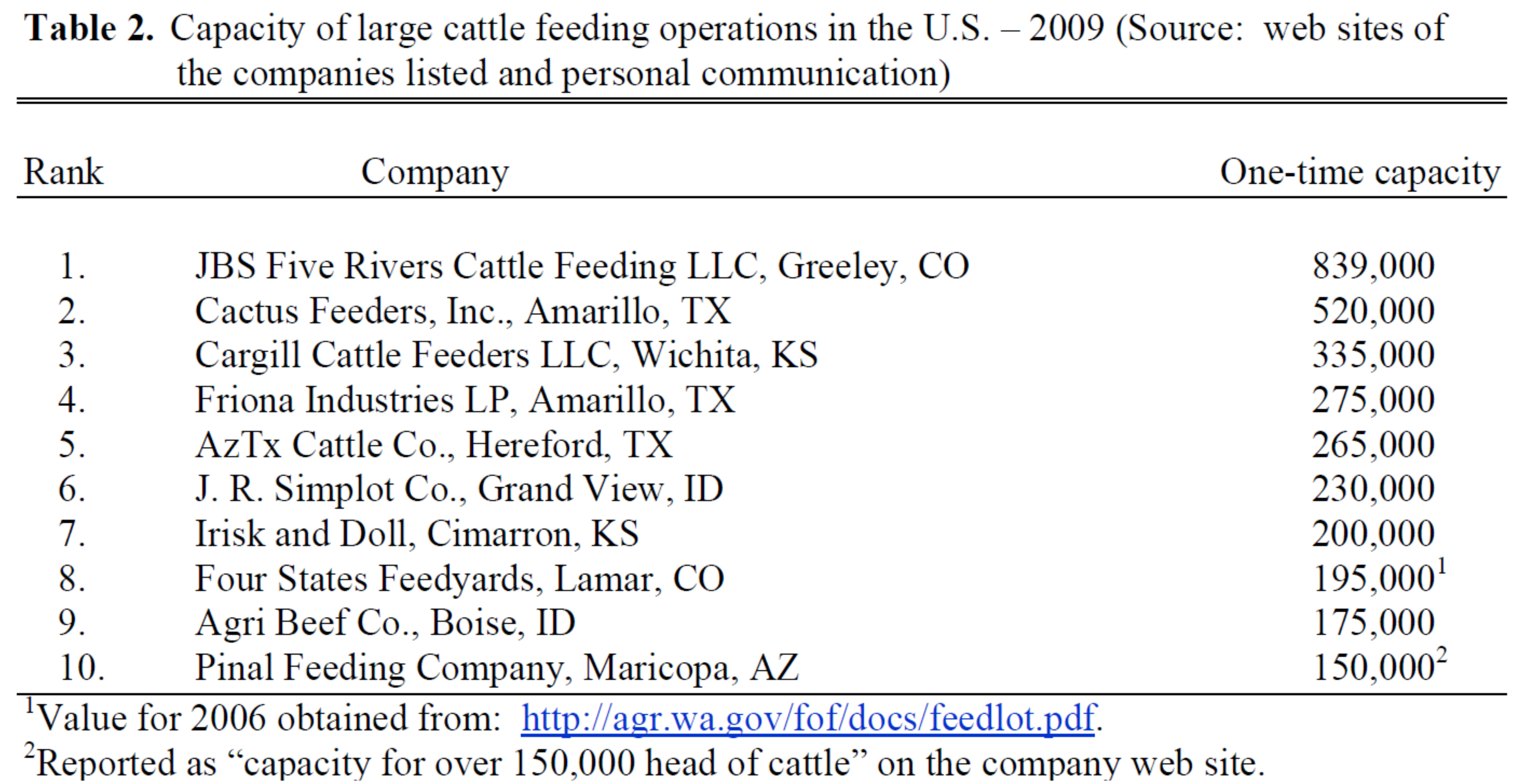


Table 2. Capacity of large cattle feeding operations in the U.S. – 2009 (Source: web sites of the companies listed and personal communication)

Rank	Company	One-time capacity
1.	JBS Five Rivers Cattle Feeding LLC, Greeley, CO	839,000
2.	Cactus Feeders, Inc., Amarillo, TX	520,000
3.	Cargill Cattle Feeders LLC, Wichita, KS	335,000
4.	Friona Industries LP, Amarillo, TX	275,000
5.	AzTx Cattle Co., Hereford, TX	265,000
6.	J. R. Simplot Co., Grand View, ID	230,000
7.	Irisk and Doll, Cimarron, KS	200,000
8.	Four States Feedyards, Lamar, CO	195,000[1]
9.	Agri Beef Co., Boise, ID	175,000
10.	Pinal Feeding Company, Maricopa, AZ	150,000[2]

[1] Value for 2006 obtained from: http://agr.wa.gov/fof/docs/feedlot.pdf.

[2] Reported as "capacity for over 150,000 head of cattle" on the company web site.

http://ag.arizona.edu/ANS/swnmc/Proceedings/2010/06_Galyean_2010.pdf

Potential uses and value of genomic information for different sectors of the cattle industry

Use	Seedstock	Commercial	Feedlot	Processor
DNA-assisted selection	XXXX	X	XXXX	XXXX
Parentage	XX	X		
Recessive allele testing	XX	X		
Control of Inbreeding	XX	X		
Mate selection	XX	X		
DNA-assisted management/purchasing		X	XX	XX
Product differentiation				XXXX
Traceability				XX
Vet med. diagnostics - the “diagnomics” age?	X	X	XX	X

The Future
NEXT EXIT

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 (http://www.brdcomplex.org)
  - 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 200 cattle from up to 10 different beef breeds
  - $3 million, 5 year project; Jan 2013 – December 2017

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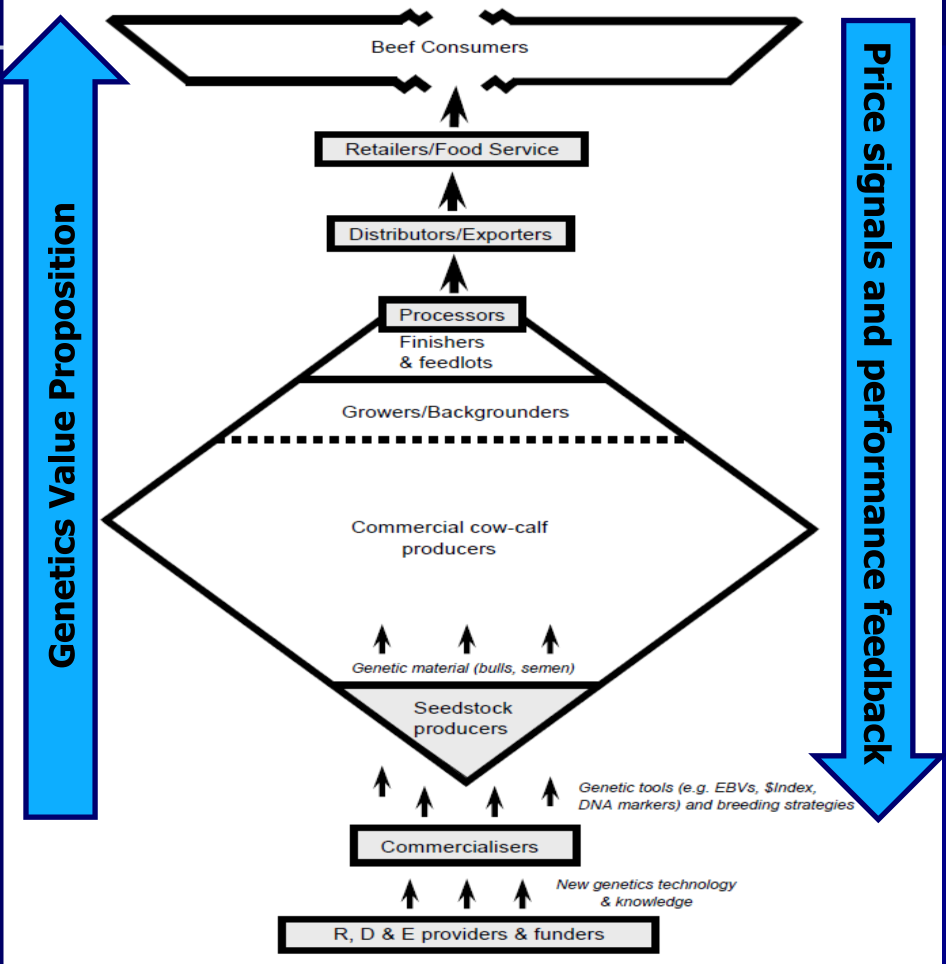
No one said we are targeting the low hanging fruit

Industry structure may evolve to enable the exchange of information and value between the different sectors.



For widespread technology adoption, breeders need to be adequately rewarded for making DNA investments and selection decisions for traits that benefit the different sectors of the beef industry.

Parnell, P.F. 2007. Effective value chain partnerships are essential for rapid adoption of beef genetics technology. Association for the Advancement of Animal Breeding and Genetics. 18. 167-174 .

Potential uses of genomic information for beef sectors

ONLY THESE SECTORS PRODUCE NEW ANIMALS

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

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 Sector	Type of DNA product // DNA information access required	Cost?? ($US)
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	2013	2020
• single marker/ single trait • reported genotypes • single marker accounted for small amount of genetic variation • limited adoption • technology oversold	• 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 are available for calibration/validation	• universal 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

CONCLUSIONS

- Genomics has the potential to enable selection for novel traits
- Need large training populations to develop genetic evaluations for novel traits
- USDA National Institute of Food and Agriculture has recently funded three large 5-year, multi-institution grants on genomic approaches to feed efficiency, fertility and reduced BRD susceptibility
- These projects employ high-density genotyping of large numbers of phenotyped animals
- Need to derive relative economic value of these traits to incorporate them into a selection index that appropriately weights these traits based on their economic value

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 rapidly-declining 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.

Questions?

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