Biotech Beef and Cloned Cows: Does Animal Biotechnology have a Future?

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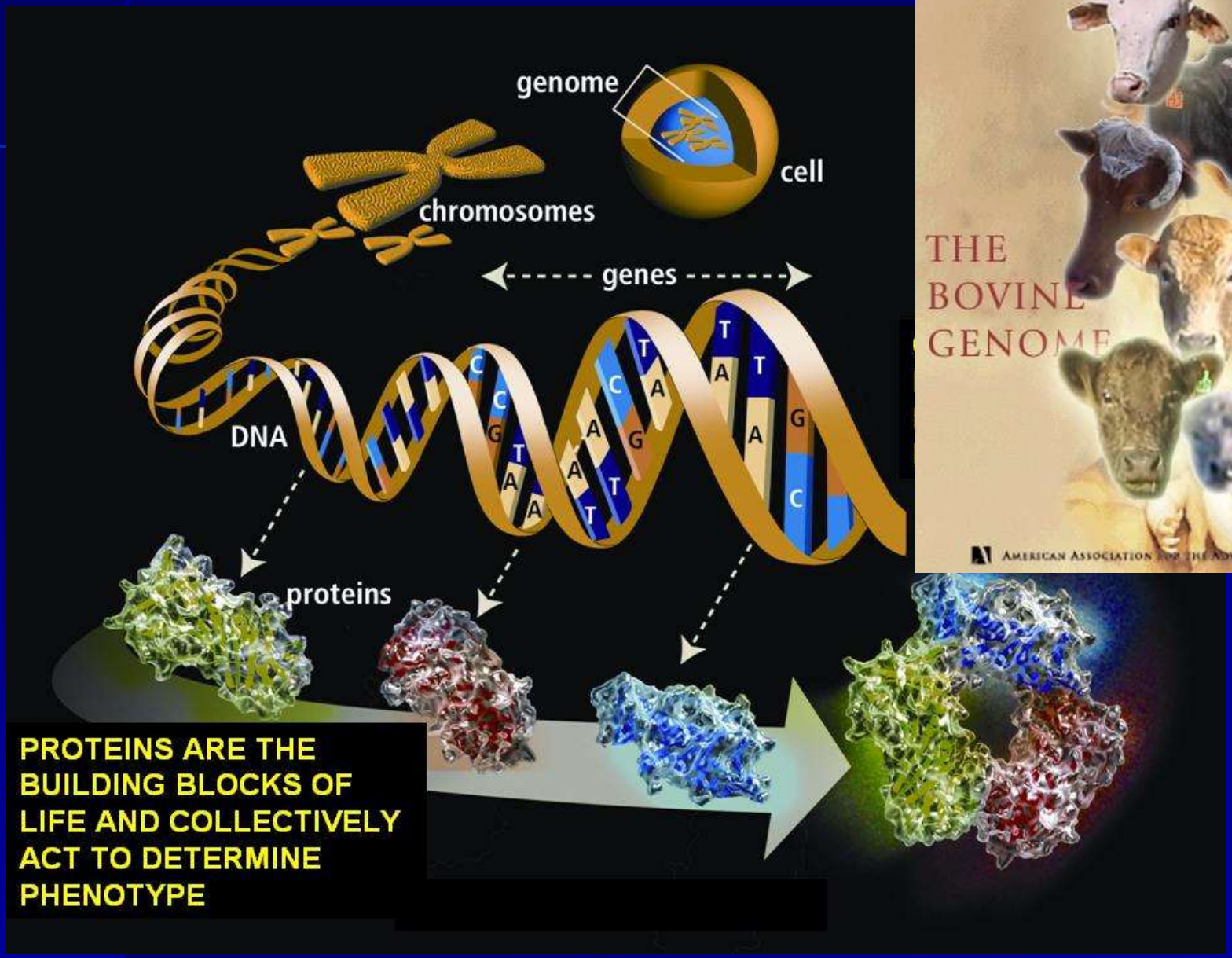
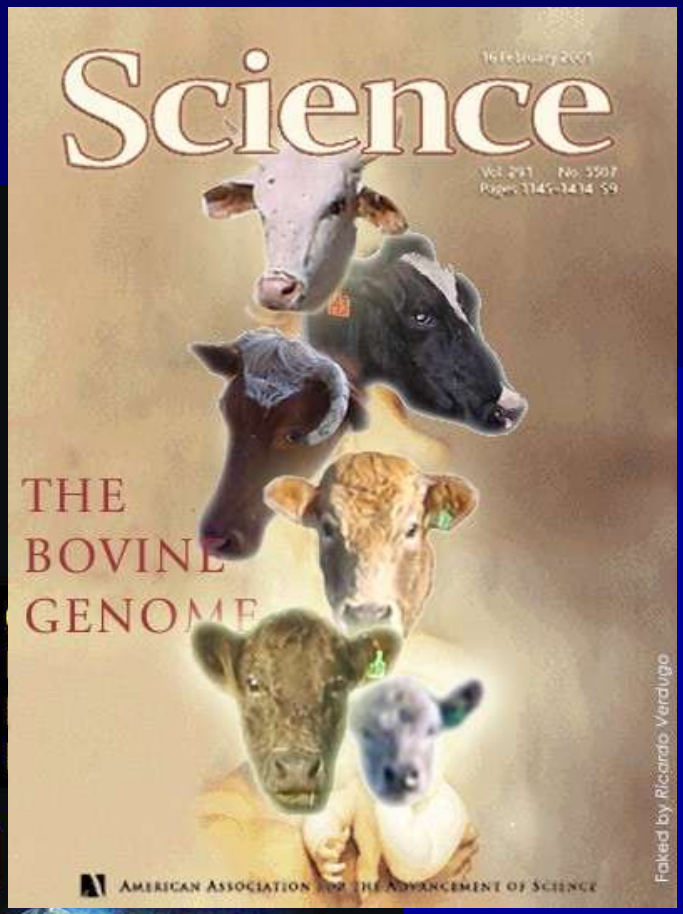
Animal breeders can influence the rate of genetic gain by altering components of the "breeders" equation:

$$\Delta G = \frac{\textit{intensity of selection } X \textit{ accuracy of selection } X \sqrt{\textit{genetic variance in population}}}{\textit{generation interval}}$$

DNA information offers new opportunities for breeders!





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

GeneSTAR SureTRAK SireTRACE GeneSTAR Pfizer Pfizer Animal Genetics

igenity

ImmGen.

genmark

QUANTUM GENETICS
DNA Assisted Feedlot Management

GENETICVISIONS

GENESEEK
Molecular Solutions for Breeding and Genetics

ANGUSURE

PRESCRIBE GENOMICS

MMI GENOMICS, INC.
BREED-TRU
DNA VERIFIED

METAMORPHIX, INC.

Marker-assisted selection (MAS)

The process of using the results of DNA-marker testing to predict the **genetic merit** of the animal being tested and assist in the selection of individuals to become parents in the next generation.

Tests for quantitative traits – before 2010 10-100 SNPs

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

GeneSTAR RESULTS LEGEND

EXAMPLE REPORT - *GeneSTAR EXAMPLE Results* - **EXAMPLE REPORT**

Animal ID	Gender	Bar Code	Breed		RESULTS	GPD™
ABC	F	426732999	Simmental	Quality Grade	QG1 ★★ QG2 ★★ QG3 ★★ QG4 ★★	33.86%
Reg No:	1234578					
Reg Name:	Example Animal ABC		☐ Publication	Tenderness	T1 ★★ T2 ★★ T3 ★★	-2.2 lbs
				Feed Efficiency	FE1 ★★ FE2 ★★ FE3 ★★ FE4 ★★	-3.96 lbs
				GeneSTAR Black	EDED	HB

GeneSTAR Black Standard Result

	Result	Symbol
Homozygous Black Result	**EDED**	**HB**
The following results are not Homozygous Black:		
Most likely Black Coated, Red Carrier	EDe	not HB
Most likely Black Coated, Wild Type Carrier	E+ED	
Most likely Red Coated, Wild Type Carrier	E+e	
Most likely Red Coated, Double Red Carrier	ee	
Any Color Likely, Double Wild Type	E+E+	

GeneSTAR Quality Grade (QG1, QG2, QG3 and QG4) - Presented as the result of the four Quality Grade markers:

*STAR Values – Indicate the value for each **Quality Grade** genes.*

0 Indicates the animal has 0 copies of the favorable gene

★ Indicates the animal has 1 copy of the favorable gene

★★ Indicates the animal has 2 copies of the favorable gene

RP Indicates one or both of the values is still pending.

NR No result due to insufficient or poor quality sample.

Quality Grade GPD - For Quality Grade markers, a GPD™ is reported as the ***increased*** likelihood that a carcass will grade Choice or better, and is derived from independent third party validation results. The animal in the EXAMPLE REPORT with two Stars for QG1and QG2 and 0 stars for QG3 and QG4 would be 13.46% more likely to have a Choice or better Quality Grade over an animal with no Quality Grade markers. For this animal the Quality Grade GPD™ would be +13.46.

GeneSTAR Tenderness (T1, T2, and T3) - Presented as the result combination of the three Tenderness markers:

*STAR Values – Indicate the value for each **Tenderness** gene*

0 Indicates the animal has 0 copies of the favorable gene

★ Indicates the animal has 1 copy of the favorable gene

★★ Indicates the animal has 2 copies of the favorable gene

RP Indicates one or both of the values is still pending.

NR No result due to insufficient or poor quality sample.

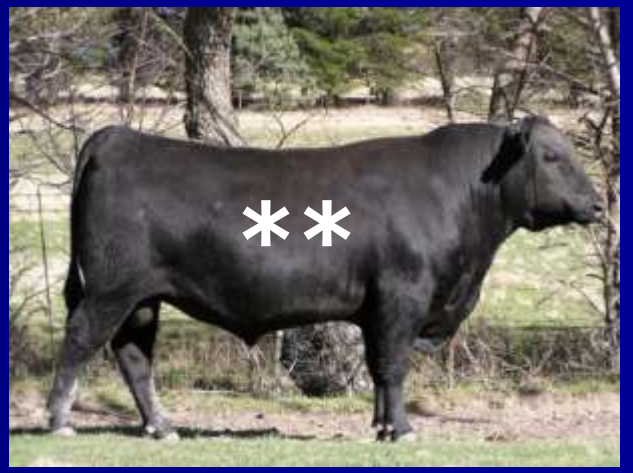
Tenderness GPD - The numerical value for GeneSTAR® Tenderness is reported in lbs of shear force (WBSF) and represents a reduction in the shear force required to cut a steak. It is derived from independent third party validation results. The animal in the EXAMPLE REPORT with two Stars for T1, zero Stars for T2, and zero Stars for T3 would require 0.7 pounds less shear force to cut a steak as compared to an animal with no markers for Tenderness. Thus, the Tenderness GPD™ would be -0.7.

GeneSTAR Feed EfficiencyTenderness (FE1, FE2, FE3, and FE4) - Presented as the result of the four Feed Efficiency markers:

*STAR Values – Indicate the value for each **Feed Efficiency** gene*

Which would you rather have???

- A bull that is ‘homozygous’ for a positive genetic variant with a low-accuracy EPD of +3, or
- Or an unrelated bull carrying no copies of that genetic variant with a low-accuracy EPD of +3



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 is wrong with the current model ?

- A few markers are not sufficient to account for much (>10%) of the additive genetic variation
- Unclear how to combine stars with EPD information – which one should be given more weighting?
- Markers do not exist for many important traits
- Early adopters of genotyping for MAS in livestock have not experienced sufficient value capture i.e. they are too expensive !

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

Genomic selection

Alternative is to trace all segments of the genome with markers

- Divide genome into 50,000 chromosome segments based on marker intervals
- Capture all QTL = all genetic variance
- Marker density must be sufficiently high to ensure that all quantitative trait loci (QTL) are in linkage disequilibrium (LD) with a marker

Implementation of Genomic Selection

r_0

Validation:
New Progeny Tested Bulls

Training 1:
Old Progeny Tested Bulls

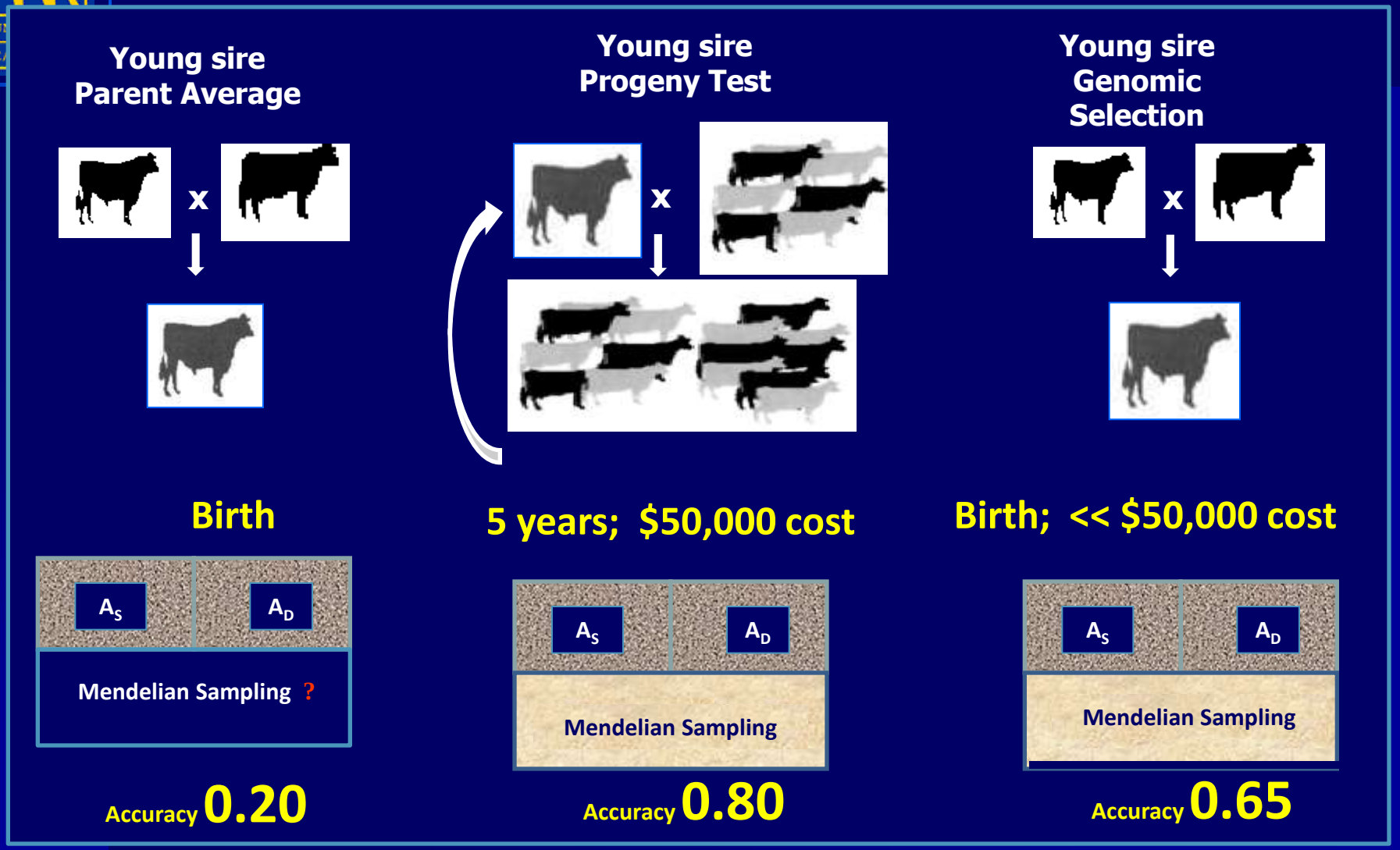
Training 2:
Old & New Progeny Tested Bulls

r_1

Application:
New Sire Candidates

Slide courtesy of Marc Thallman, US MARC

Breeding value prediction in Dairy Sires



Dairy industry suited to WGS

- 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 genotypes
- 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

Genomic selection can help breeders identify animals with superior breeding values at a young age

$$\Delta G = \frac{\textit{intensity of selection } X \textit{ accuracy of selection } X \sqrt{\textit{genetic variance in population}}}{\textit{generation interval}}$$

Genomic selection can double 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 s.d./year (progeny test)

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

i = intensity of selection

r = accuracy of selection

L = generation interval

Modified from Goddard. (2009) BIF Meeting

Velogenetics

(Georges and Massey (1991) Theriogenology 35:151-159)

- Harvest oocytes from in-utero calves
- In-vitro
  - maturation
  - fertilization
- Selection based on genetic markers
- Implant in recipient cows
- L = 6 months (0.5 instead of 6 years)

Velogenetics could increase rate of genetic gain 8X

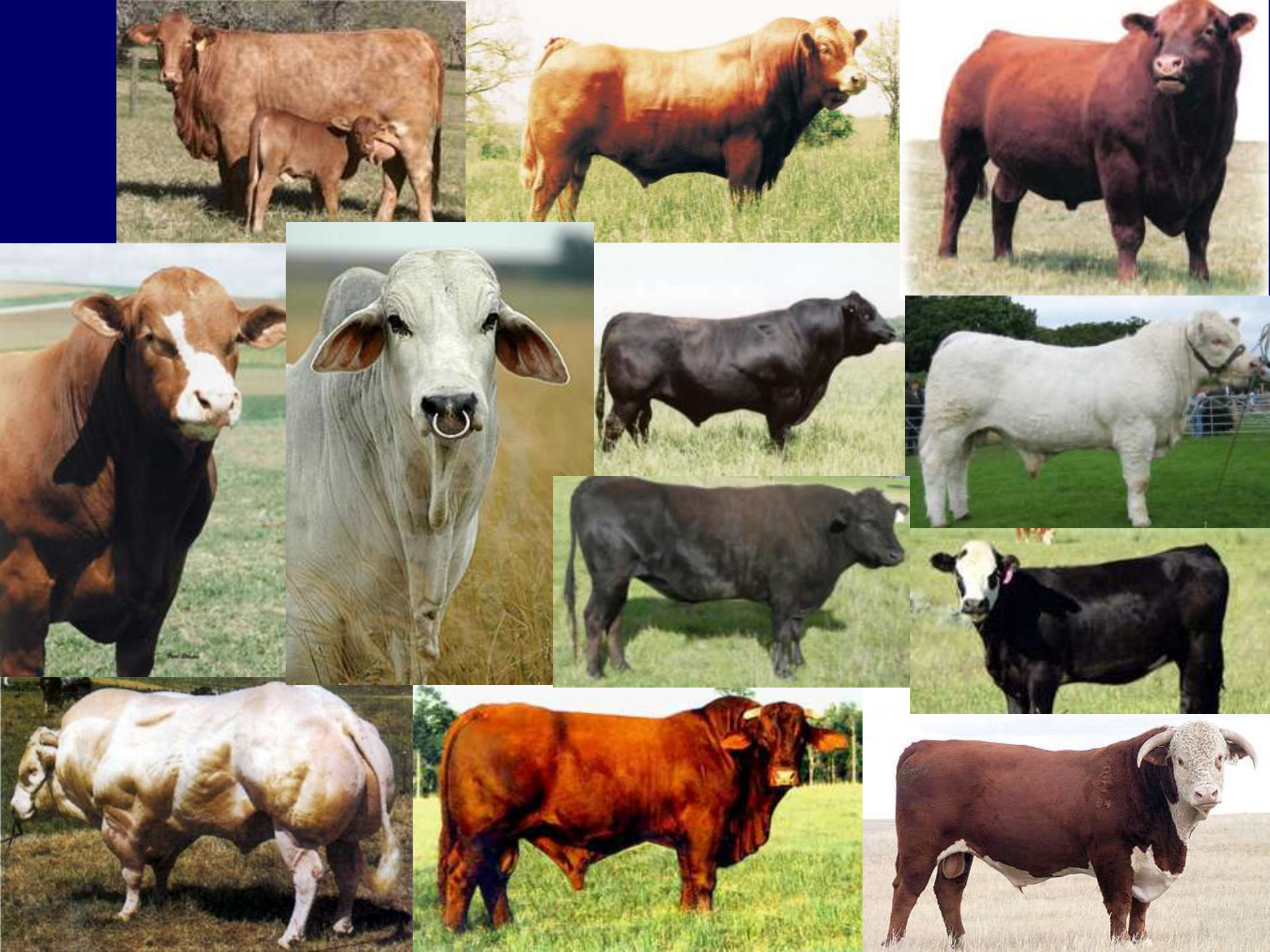
Rate of genetic gain ΔG

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

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

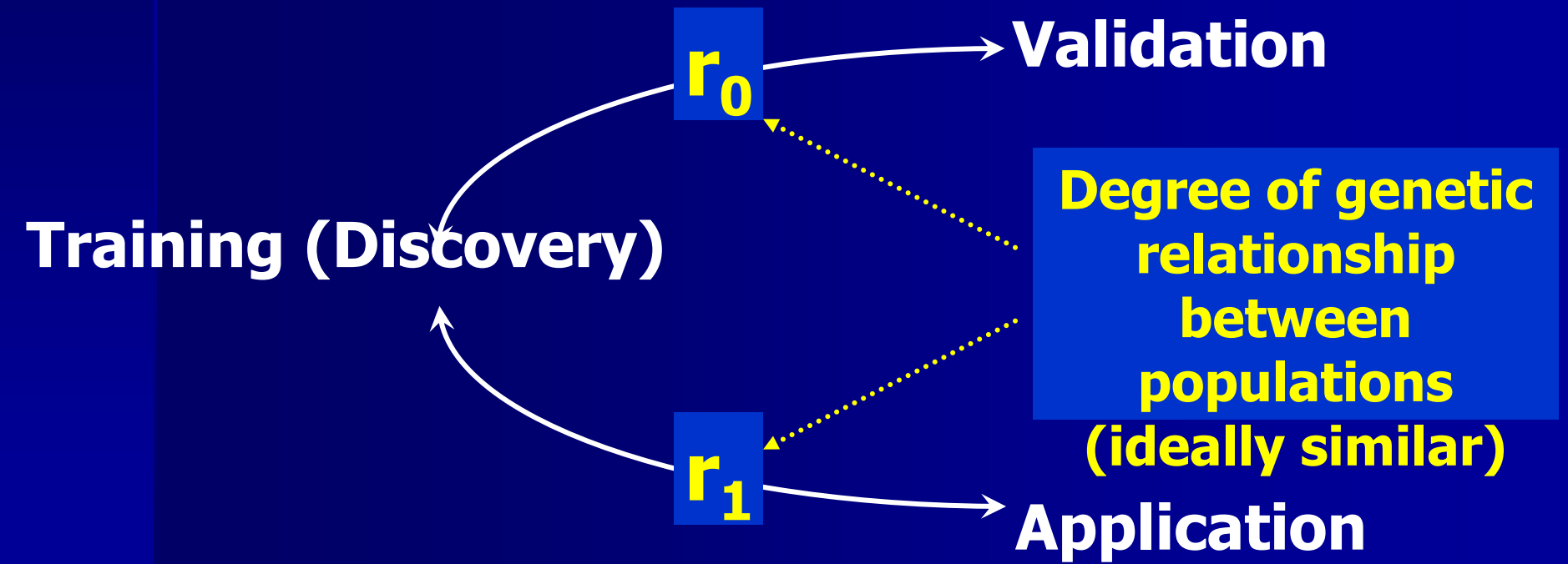
= (2*0.6 + 0.8*0.6)/ (2+2) = 0.42 (genomic selection)

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



Validation

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



Slide courtesy of Marc Thallman, US MARC

Australian Pfizer MVP Validation Results
(http://www.beefcrc.com.au/Aus-Beef-DNA-results)

This second generation of products from Pfizer involved analysis with 56 SNP markers and predictions were for a limited number of traits

PFIZER ANIMAL GENETICS Trait	h^2	% Genetic variation explained	
		Pfizer MVP sales literature (2009)	Australian Validation (2009)
Net Feed Intake	0.39	9%	0-6%
Tenderness	0.37	24%	2-30%
Marbling score	0.37	7%	0-4%

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 Animal Health
Animal Genetics

Australian 2010 50,000 SNP Validation Results

Pfizer Animal Genetics Trait	h^2	% Genetic variation explained			
		Pfizer MVP (2009)	Australian Validation (2009)	Pfizer 50K (2010)	Australian Validation (2010)
Average Daily Gain	0.28			30%	1-10%
Net Feed Intake	0.39	9%	0-6%	12%	0%
Dry matter intake	0.39			11%	4-5%
Tenderness	0.37	24%	2-30%	26%	Not evaluated
Calving Ease (Direct)	0.1			22%	6%
Birth weight	0.31			28%	12-16%
Weaning Weight	0.25			32%	12-19%
Calving ease (maternal)	0.1			40%	4%
Milking Ability	0.25			27%	10-14%
Carcass weight	0.39			29%	6-13%
Backfat thickness	0.36			40%	14-19%
Ribeye area	0.4			29%	10-20%
Marbling score	0.37	7%	0-4%	34%	4-11%

Practical implications

- How many phenotypic records are required in the initial experiment estimating the effect of chromosome segments to get accurate prediction equations?
- How many markers do you need – 50K, 800K, whole genome to make it work across breeds?
- How often do we need to re-estimate the chromosome segment effects?
- Does this technology change optimal breeding program design?
- How much can you afford to pay?

Objective

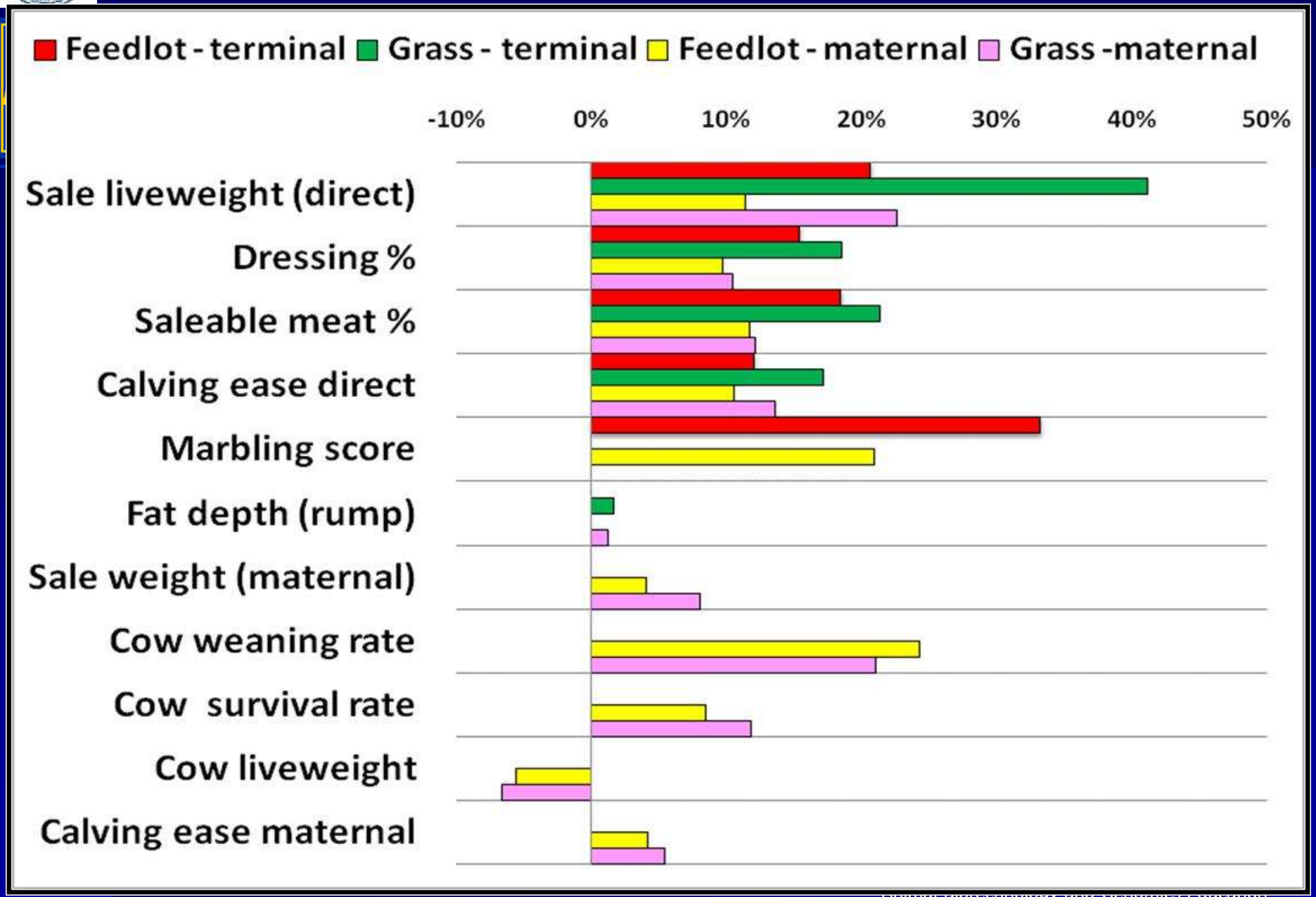
Estimate the value of using DNA test information to increase the accuracy of beef bull selection in a seedstock breeding program

- The expected returns from using a commercial sire sourced from a seedstock herd using DNA testing to improve the accuracy of selection
- Additionally, the value of marker information in the selection of replacement stud males to be mated in a seedstock breeding program was estimated.

The following seedstock operation was modeled

Parameters	Value
Number of stud cows	600
Number of bull 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**

Relative Importance of traits in the breeding objectives



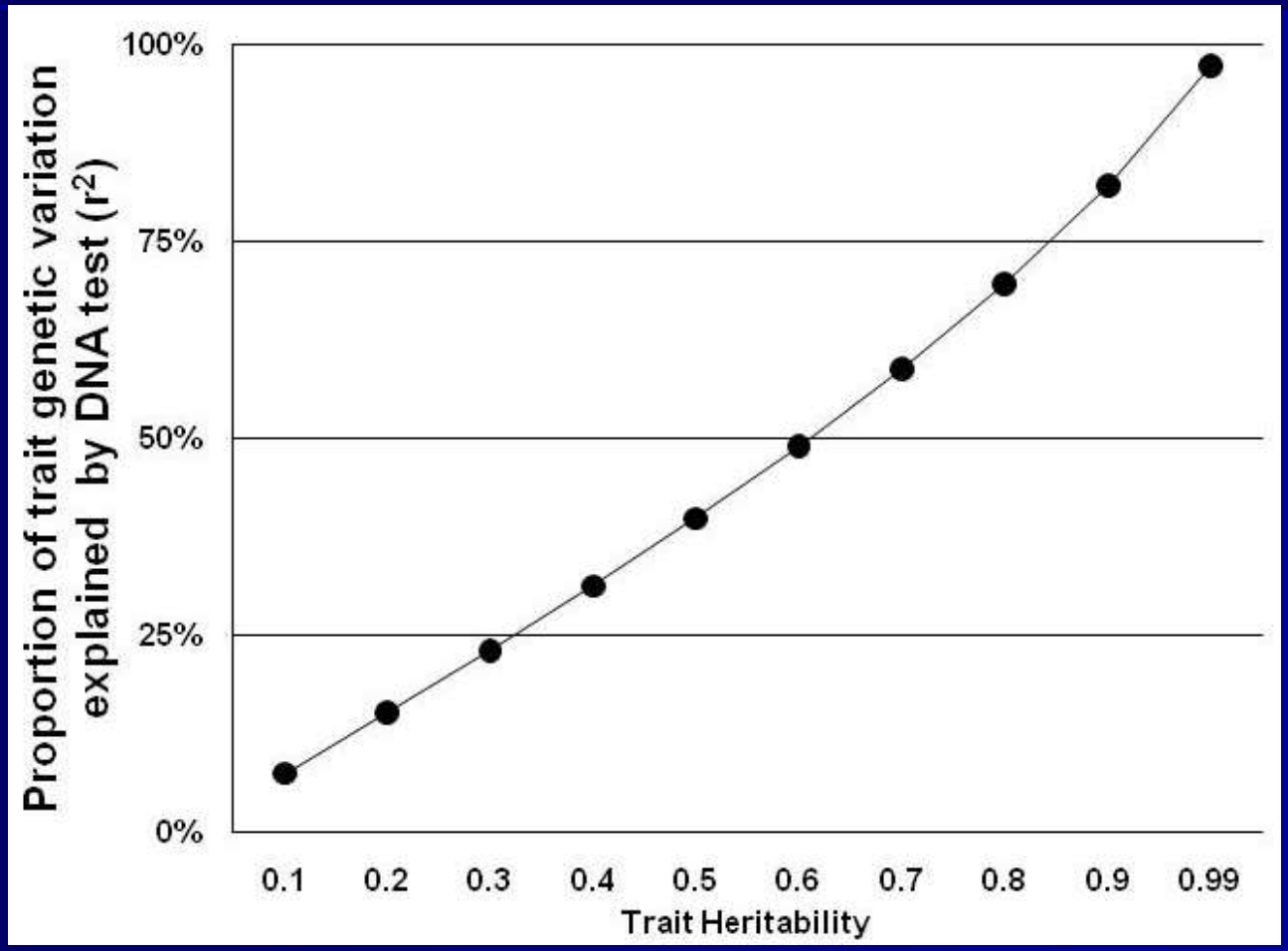
Materials and methods

- Phenotypic performance records on selection criteria were collected on the individual, sire, dam and 20 half-sibs.
- Selection index theory was used to predict the potential benefit of including DNA information to improve the accuracy of selection.
- Information from DNA test information was modeled as a molecular breeding value (q_i) explaining a proportion (ρ) of the additive genetic variance (σ_{ai}^2) in trait i; $V_{qi} = \rho.\sigma_{ai}^2$, as described by Lande and Thompson (1990).

Proportion of genetic variation explained by DNA test set to h^2 of selection criteria

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

Effect of trait heritability (h^2) on theoretical proportion of trait genetic variation explained by DNA tests trained in populations of 2500 (•) individuals with phenotypic observations*.



* Effective population size (N_e) = 100, length of bovine genome (L) = 30 M, effective number of loci (M_e) = 2NeL, and a normal distribution of QTL effects were assumed. Derived from the formula of Goddard (2009).

Materials and methods (continued)

- Indexes were constructed for four breeding objectives developed for the Australian cattle industry; and index accuracies were calculated when information source included DNA test information from one of the two DNA panels **and** performance recording, over that derived from performance recording alone.

- Discounted gene flow methodology (Hill, 1974) was used to calculate the value derived from the use of superior bulls selected using DNA test information **and/or** performance recording. Results were ultimately calculated as discounted returns per DNA test purchased by the seedstock operator.

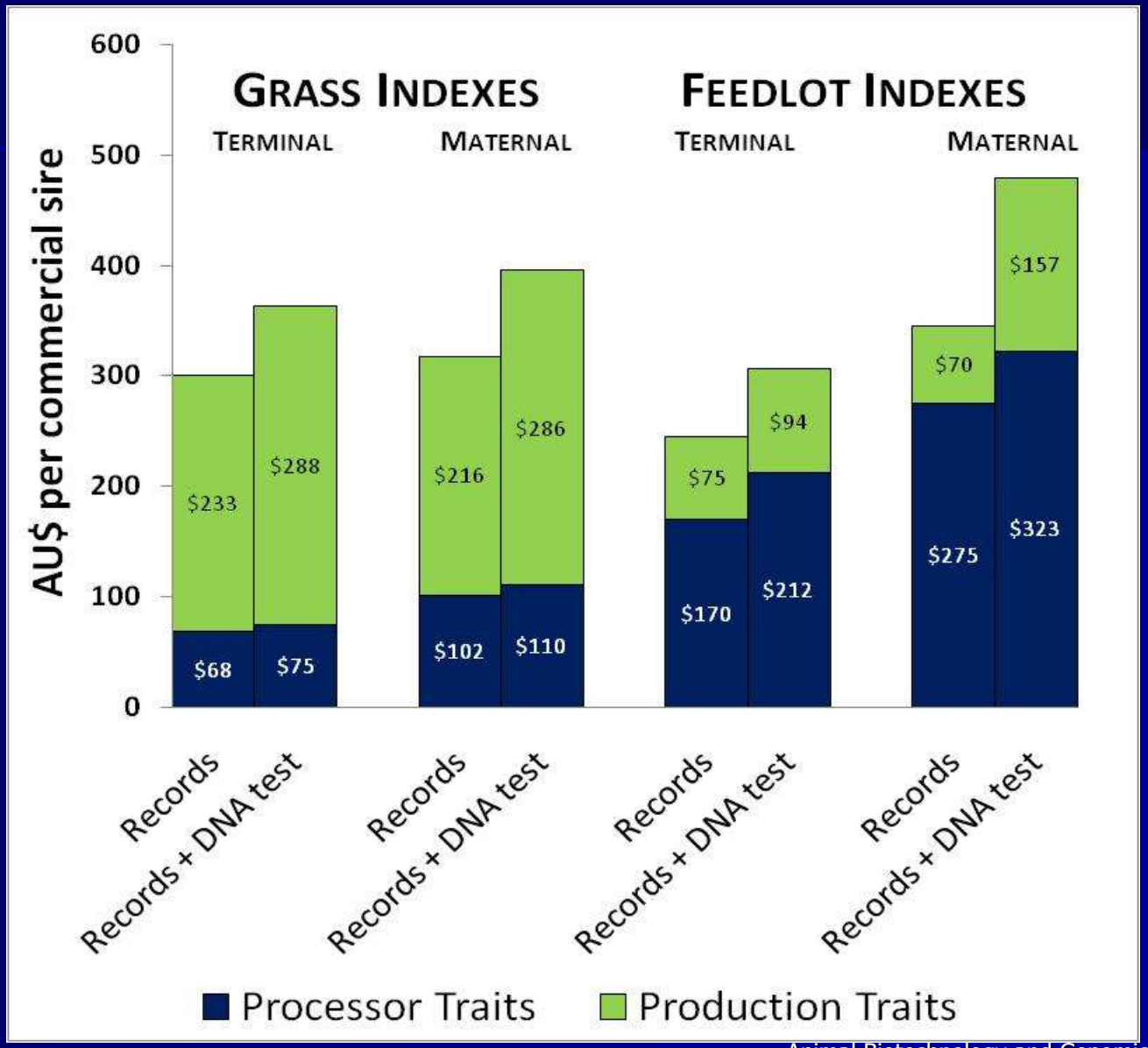
Results: Increase in index accuracy from DNA testing

Variable	Unit	Information available	GRASS INDEX		FEEDLOT INDEX	
			Terminal	Maternal	Terminal	Maternal
Accuracy of the index	r	Performance Records	**.50**	**.29**	**.26**	**.19**
		Records + DNA test	**.58**	**.35**	**.32**	**.27**

Results: Value of genetic improvement (ΔG) per COMMERCIAL bull derived from performance recording and DNA testing to increase the accuracy of selection in a closed seedstock breeding program

Variable	Unit	Information available	GRASS INDEX		FEEDLOT INDEX	
			Terminal	Maternal	Terminal	Maternal
Value of ΔG in commercial sires selected from top half of stud herd	AU$ /bull	Performance Records	**$301**	**$318**	**$245**	**$345**
		Records + DNA test	**$363**	**$396**	**$306**	**$480**

Beef industry sector where value of ΔG in improved commercial bull is derived



Results: Value of genetic improvement (ΔG) per STUD bull derived from performance recording and DNA testing to increase the accuracy of selection in a closed seedstock breeding program

Variable	Unit	Information available	GRASS INDEX		FEEDLOT INDEX	
			Terminal	Maternal	Terminal	Maternal
Value of ΔG in stud sires selected from top half of stud herd	AU$ /bull	Performance Records	**$17899**	**$15922**	**$14579**	**$16751**
		Records + DNA test	**$21617**	**$19724**	**$18211**	**$23110**

Results: Value of genetic improvement (ΔG) per DNA test in commercial and stud sires

Variable	Unit	Information available	GRASS INDEX		FEEDLOT INDEX	
			Terminal	Maternal	Terminal	Maternal
Increased value derived from ΔG in commercial sires	AU$/ DNA test	Records + DNA test	**$31**	**$39**	**$30**	**$67**
Increased value derived from ΔG in stud sires	AU$/ DNA test	Records + DNA test	**$111**	**$114**	**$109**	**$191**

Results: Combined value per DNA test (assuming a perfect market)

Variable	Unit	Information available	GRASS INDEX		FEEDLOT INDEX	
			Terminal	Maternal	Terminal	Maternal
Increased value derived from ΔG in commercial sires	AU$/ DNA test	Records + DNA test	**$31**	**$39**	**$30**	**$67**
Increased value derived from ΔG in stud sires	AU$/ DNA test	Records + DNA test	**$111**	**$114**	**$109**	**$191**
Total value per test to seedstock operator	AU$/ DNA test	Records + DNA test	**$143**	**$153**	**$139**	**$258**

Value of a multi-trait DNA test requires knowledge of:

1. Selection objective being targeted
2. Heritability of the analyzed trait (h^2)
3. Accuracy of genetic estimates already available to inform selection decisions
4. Genetic correlation between MVP and the trait (r_g)
5. Genetic variances and covariances for selection index calculations
6. Regression coefficient of phenotype on MBV (b)
7. Biological attributes and structure of stud and commercial herds
8. Selection intensity of replacement stud sires and bulls for sale (and females)
9. Number of calves per exposure
10. Type of herd (terminal, maternal)
11. Value derived from accelerated genetic progress
12. Sector where value is derived and how that is value is shared
13. Cost of test, and which animals are being tested
14. Planning horizon etc., etc., etc.

Summary of value proposition

- DNA tests trained on ~2,500 phenotpyic records increased the response to selection 20-41%
- Value of the genetic gain ranged from AU$139-258/test.
- Need independent estimates of proportion of genetic variation explained by DNA tests to calculate value
- Returns from DNA testing will be enterprise dependent
- DNA information clearly has the potential to provide value to seedstock producers if it is meaningfully incorporated into national cattle evaluations
- The commercial viability of DNA testing beef bulls will call for efficient price signalling throughout the production chain.

Lets switch gears to cloning and genetic engineering of animals

Where does cloning come into the breeders equation?

$$\Delta G = \frac{\textit{intensity of selection } X \textit{ accuracy of selection } X \sqrt{\textit{genetic variance in population}}}{\textit{generation interval}}$$

Where does genetic engineering come into the breeders equation?

$$\Delta G = \frac{\text{intensity of selection } X \text{ accuracy of selection } X \sqrt{\text{genetic variance in population}}}{\text{generation interval}}$$

"I know it when I see it"

Of the people who say they know nothing about biotechnology, genetic engineering or genetic modification; almost half (46%) disapprove of the use of genetic modification to create plant-based foods, and 66% disapprove of animal-based genetic modification.

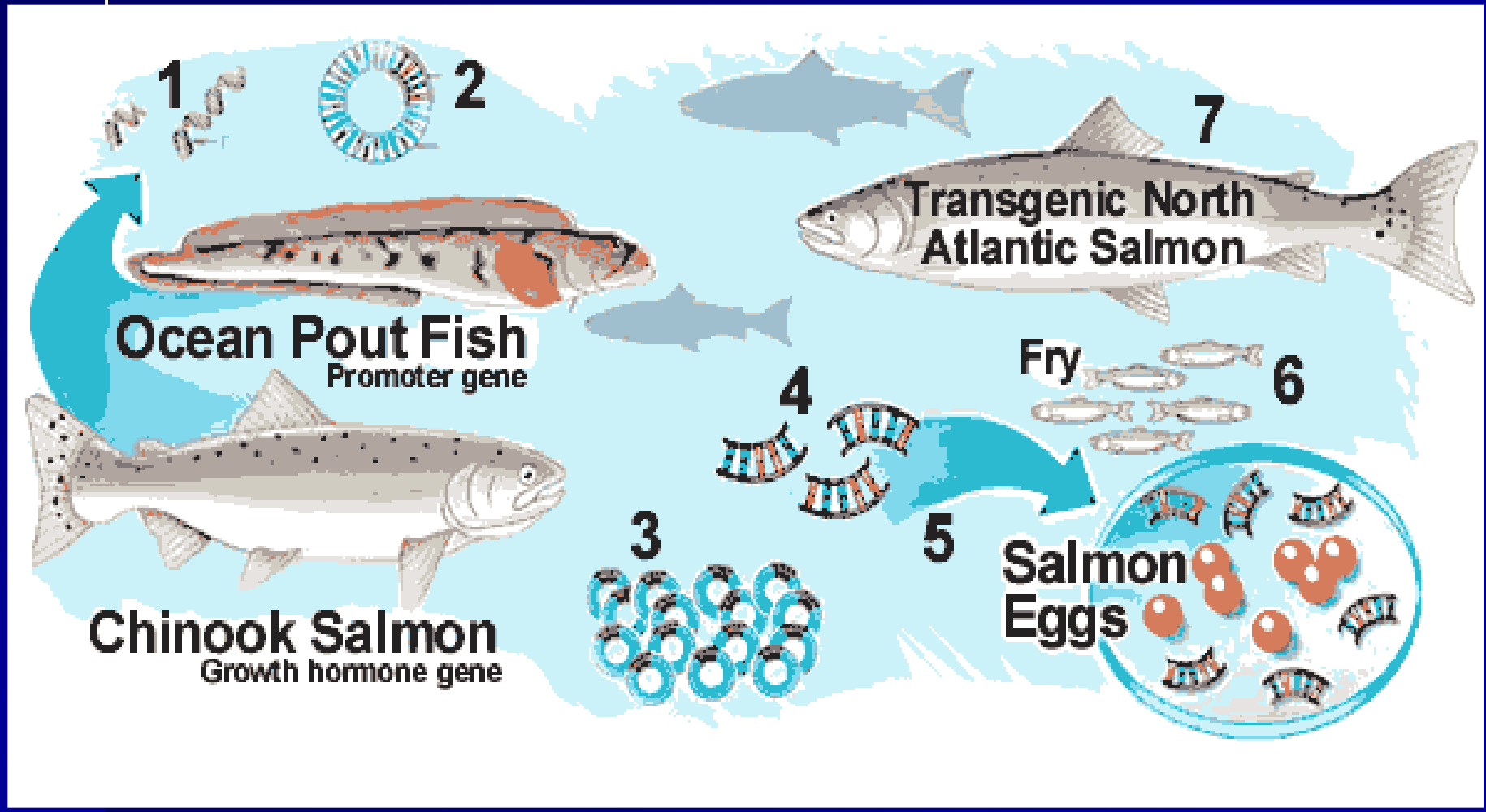
Hallman, W. K., Hebden, W. C., Aquino, H.L., Cuite, C.L. and Lang, J.T. 2003. *Public Perceptions of Genetically Modified Foods: A National Study of American Knowledge and Opinion.* Rutgers - The State University of New Jersey.

Thank goodness we have not been genetically modifying animals up until this point…..






Let us consider the case of the Aquabounty salmon



Product Definition for the AquAdvantage Salmon

Product Identity

Triploid hemizygous, all-female Atlantic salmon (*Salmo salar*) bearing a single copy of the α-form of the opAFP-GHc2 rDNA construct at the α-locus in the EO-1α lineage.

Claim

Significantly more of these Atlantic salmon grow to at least 100 g within 2700 deg C days than their comparators.

Limitations for Use

These Atlantic salmon are produced as eyed-eggs for grow-out only in the FDA-approved physically-contained fresh water culture facility.

Alison Van Eenennaam , Ph.D., UC Davis

FDA NEWS RELEASE

FOR IMMEDIATE RELEASE
January 15, 2009

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Michael Herndon, (301) 796-4673
Consumer Inquiries:
888-INFO-FDA

FDA Issues Final Guidance on Regulating Genetically Engineered Animals

En Español

The U.S. Food and Drug Administration today issued a final guidance for industry on the regulation of genetically engineered (GE) animals under the new animal drug provisions of the Federal Food, Drug and Cosmetic Act (FFDCA). The guidance, titled "The Regulation of Genetically Engineered Animals Containing Heritable rDNA Constructs," clarifies the FDA's statutory and regulatory authority, and provides recommendations to producers of GE animals to help them meet their obligations and responsibilities under the law.

Genetic engineering generally refers to the use of recombinant DNA (rDNA) techniques to introduce new characteristics or traits into an organism. When scientists splice together pieces of DNA and introduce a spliced DNA segment into an organism to give the organism new properties, it is called rDNA technology. The spliced piece of DNA is called the rDNA construct. A GE animal is one that contains an rDNA construct intended to give the animal new characteristics or traits.

"Genetic engineering is a cutting edge technology that holds substantial promise for improving the health and well being of people as well as animals. In this document, the agency has articulated a scientifically robust interpretation of statutory requirements," said Randall Lutter, Ph.D., deputy commissioner for policy. "This guidance will help the FDA efficiently review applications for products from GE animals to ensure their safety and efficacy."

The FDA released the draft guidance in September 2008 with a 60-day public comment period, and received about 28,000 comments. The agency has summarized and responded to these comments on the Web site listed below.

The FDA's Center for Veterinary Medicine (CVM) has been working with developers of GE animals on both early stage and more mature applications.

"At this time, it is our intent to hold public scientific advisory committee meetings prior to making decisions on GE animal-related applications" said Bernadette Dunham, D.V.M., Ph.D., director of CVM.

The FFDCA defines "articles (other than food) intended to affect the structure or any function of the body of man or other animals" as drugs. An rDNA construct that is in a GE animal and is intended to affect the animal's structure or function meets the definition of an animal drug, whether the animal is intended for food, or used to produce another substance. Developers of these animals must demonstrate that the construct and any new products expressed from the inserted construct are safe for the health of the GE animal and, if they are food animals, for food consumption.

The guidance also describes the manufacturer's responsibility in meeting the requirements for environmental review under the National Environmental Policy Act.

For more information:

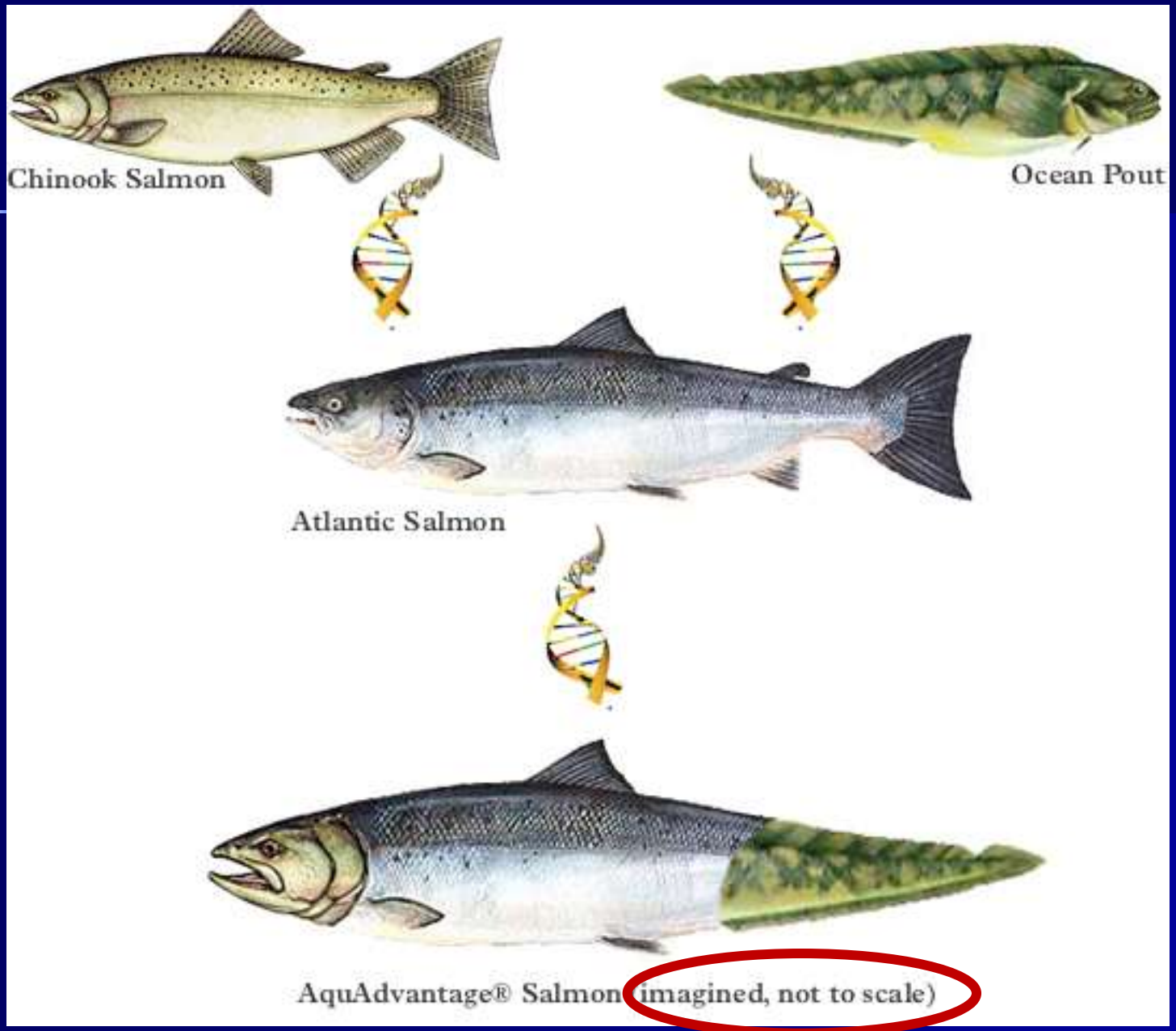
- Genetically Engineered Animals

FDA public Veterinary Medicine Advisory Committee (VMAC) Meeting was held September 19-20th, 2010
Labeling meeting was held September 21st, 2010

Van Eenennaam 11/11/2010

What the AquaAdvantage salmon actually looks like….

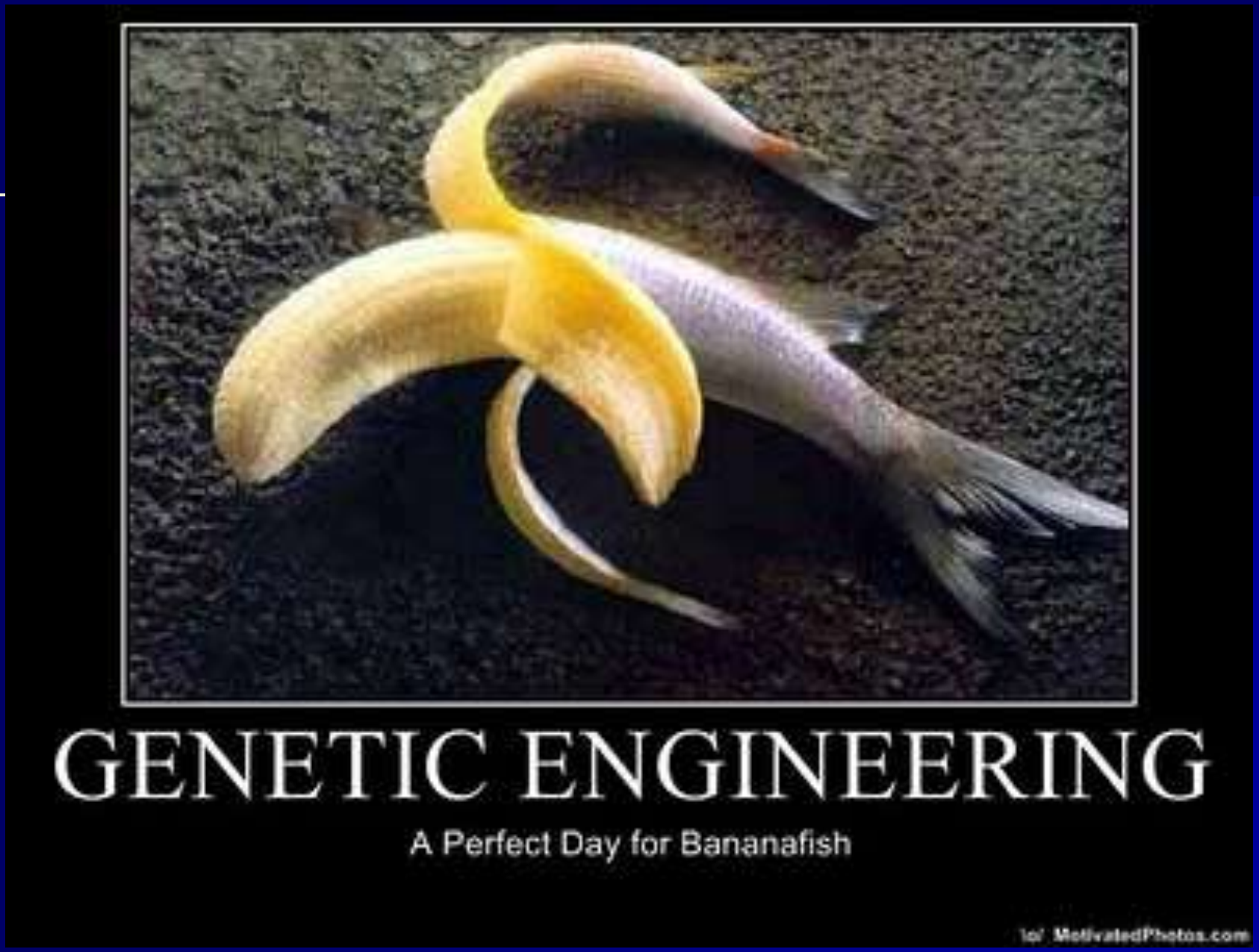
Retrieved from "AquAdvantage" image search on web



Retrieved from "AquAdvantage" image search on web

Frankenfish

Retrieved from "AquAdvantage" image search on web



SCIENCE

Frankenfood, Coming Soon to a Store Near You?

Published September 20, 2010 | FoxNews.com

Print Email Share Comments (0) Recommend 799 Text Size

Reuters/Barrett & McKay Photo/AquaBounty Technologies

A genetically engineered AquAdvantage Salmon (background) is compared to an Atlantic salmon of the same age (foreground). The U.S. Food and Drug Administration will hold a two-day meeting starting September 19 to discuss whether to approve the altered fish for U.S. consumers to eat.

WASHINGTON – Watch for a new section between "frozen foods" and "organic" in your supermarket: genetically engineered. That is, if the government approves the so-called "frankenfoods" for sale.

The Food and Drug Administration Monday began a two-day look at the issue Monday, focusing on genetically modified salmon, which would be the first such food approved for human consumption.

The agency has already said the salmon, which grow twice as fast as conventional ones, are safe to eat. But salmon act as a genetic gatekeeper in this case: Approve them and open the door for a variety of other genetically engineered animals, including an environmentally friendly pig that is being developed in Canada or cattle that are resistant to mad cow disease.

"For future applications out there the sky's the limit," said David Edwards of the Biotechnology Industry Association. "If you can imagine it, scientists can try to do it."

BUSINESS | OCTOBER 1, 2010

Industry Fights Altered Salmon

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By ALICIA MUNDY And BILL TOMSON

The fishing industry and politicians from commercial-fishing states are mobilizing against a possible Food and Drug Administration approval of genetically modified salmon for the American dinner table.

"Putting unlabeled, genetically altered salmon in the marketplace is simply irresponsible, and the FDA needs to strongly consider what impacts this will have before they approve this Frankenfish," Sen. Lisa Murkowski, a Republican from Alaska, said Thursday.

View Full Image

Associated Press

Icy Bay crewmen remove sockeye salmon from their net in July. Commercial fisheries are fighting the introduction of genetically altered salmon.

The resistance could raise difficulties for the FDA, whose scientists have said the AquAdvantage Atlantic salmon developed by AquaBounty Technologies Inc. is safe for human consumption. AquAdvantage contains a growth-hormone gene from another salmon that helps it grow twice as fast as conventional farmed fish.

A coalition that includes Pacific Coast trollers, Atlantic fishing companies and organic-yogurt maker Stonyfield Farm says the genetically altered salmon might threaten their livelihoods by spreading unease about salmon and other foods.

"This stuff is not healthy for people, and it's not like our fresh fish," said Angela Sanfilippo, president of the Gloucester Fishermen's Wives Association of Massachusetts.

Ms. Sanfilippo's group and others have joined with 39 lawmakers who wrote to the FDA this week asking the agency to stop its approval process for the genetically modified salmon. They cited concerns about "human health and environmental risks" from the AquAdvantage salmon.

United States Senate
WASHINGTON, DC 20510

September 28, 2010

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993

Dear Commissioner Hamburg:

We the undersigned members of the United States Senate request you halt all proceedings related to the U.S. Food and Drug Administration (FDA) approval of the first genetically engineered (GE) animal for human consumption – a hybrid salmon produced by AquaBounty Technologies. There are a number of serious concerns with the current approval process and many potential human health and environmental risks that are associated with producing GE fish have not been fully or openly reviewed. Critical information has been kept from the public and consequently, only FDA and AquaBounty know important details about the approval process for this GE salmon, or the product itself. Accordingly, we urge you to discontinue the FDA's approval process of the GE salmon at this time to protect consumers, fishing and coastal communities, and the environment.

AquaBounty's GE product is a transgenic Atlantic salmon egg, in which genes from an ocean pout have been inserted into the genes of Chinook salmon, and then inserted into an Atlantic salmon. The egg is meant to produce a fish that grows to full size twice as fast as a normal Atlantic salmon. The eggs are intended for sale to aquaculture companies which will grow them to market-sized fish to be sold for human consumption.

One of the most serious concerns regarding AquaBounty's application is the FDA has no adequate process to review a GE animal intended as a human food product. FDA is considering this GE fish through its process for reviewing a new drug to be used by animals, not for creation of a new animal, especially one intended for human consumption. Clearly, this is inappropriate. Creation of a new genetically engineered species should not be treated as an animal drug issue but undergo formal evaluation by FDA's Center for Food Safety and Applied Nutrition to review the product's potential health effects on humans.

Such a limited review of the first GE animal for human consumption is wholly inadequate to review potential public safety concerns associated and recklessly and needlessly endangers consumer health. A recent *New York Times* article reported, "the engineered salmon have slightly higher levels of insulinlike growth factor," and "some

This letter was signed by 11 Senators, and a similar one was signed by 29 members of Congress

Higher levels of insulinlike growth factor!

My reflections on the process

The VMAC participated in a candid, transparent discussion of the data. While such scientific discussions are rarely entertaining enough to make the nightly news, I consider that there was a sincere attempt to fairly and impartially evaluate the data presented

Unfortunately others used this important occasion to unfairly misrepresent the data. There is little benefit to society if attempts to increase public participation and transparency in the regulatory process provide an unfettered opportunity to demonize technology and undermine the science-based regulatory review process.

In my opinion, this process seriously jeopardized the future of genetically-engineered animals in the United States, both for food and pharmaceutical applications, with global implications.

CASE STUDY

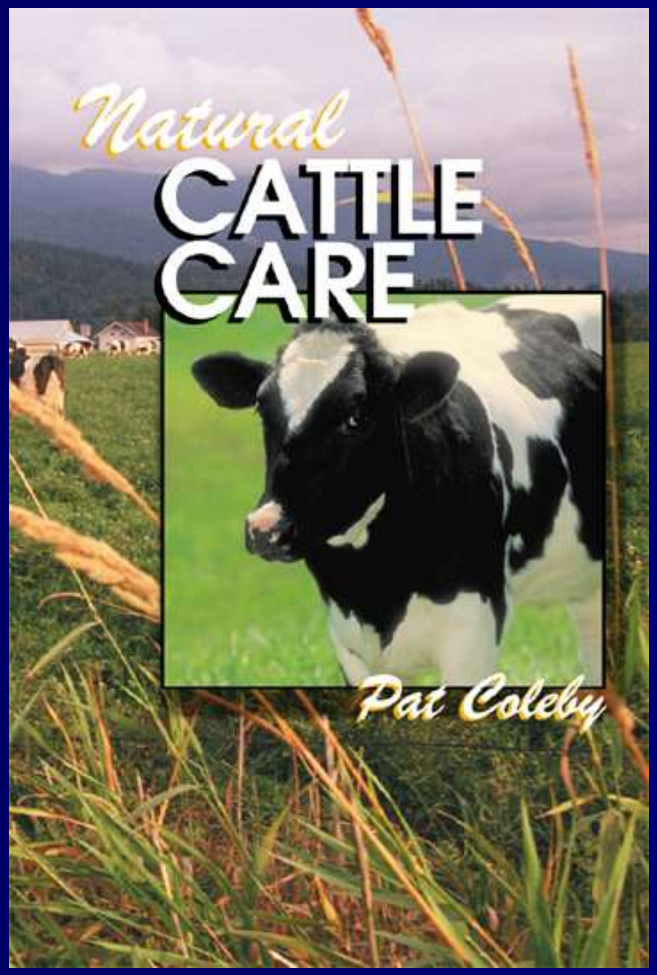
Should we genetically engineer animals improved health and welfare? If we can genetically enhance disease resistance – are we obligated to do so – and if not why not?

CASE STUDY: MASTITIS

inflammation of the mammary gland

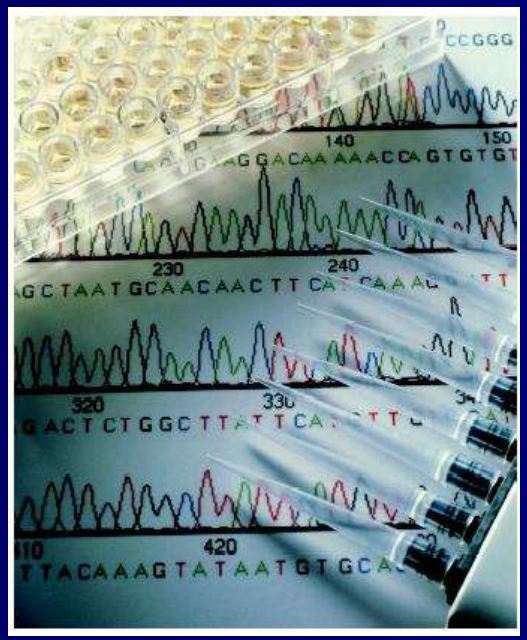
1. Conventional: Antibiotic therapy

2. Natural: alternative therapy



"An infected cow should be given an extra tablespoon of dolomite night and morning until the infection clears. Hydrogen peroxide; 10 ml squirted straight into the affected quarter has cured black mastitis in hours."

3. Genomic Selection (DNA-informed selective breeding on a grand scale)



The use of 50,000 SNP markers across the entire genome enables an estimation of genetic merit

Can be used to predict genetic merit for mastitis resistance

4. Genetic Engineering: Transgenic cows show resistance to mastitis.

USDA United States Department Of Agriculture
Agricultural Research Service

ars

Transgenic Cows Resist Mastitis-Causing Bacteria

By Rosalie Marion Bliss
April 4, 2005

WASHINGTON, April 4--U.S. Department of Agriculture researchers have used gene-transfer te
called mastitis.

"This research is an important first step in understanding how genes can be used to protect anim
Research Service (ARS).

This scientific discovery, published in the current edition of Nature Biotechnology, demonstrates t
Currently, vaccines, antibiotics and a cow's own immune system cannot effectively fight the bacte

A scientific team led by Robert J. Wall, an animal physiologist with the ARS Biotechnology and Ge
produced using recombinant DNA technology--that includes the genetic code for producing a natu

While all milk contains several naturally occurring antimicrobial proteins, such as lysozyme and la

Wall,R.J. *et al.* Genetically enhanced cows resist intramammary Staphylococcus aureus infection. *Nature Biotechnology* 23, 445-451 (2005).

5. Clone a bull whose daughters are very mastitis resistant and use these bulls to breed for mastitis resistance.

Which Animal Biotechnology would you use?

30

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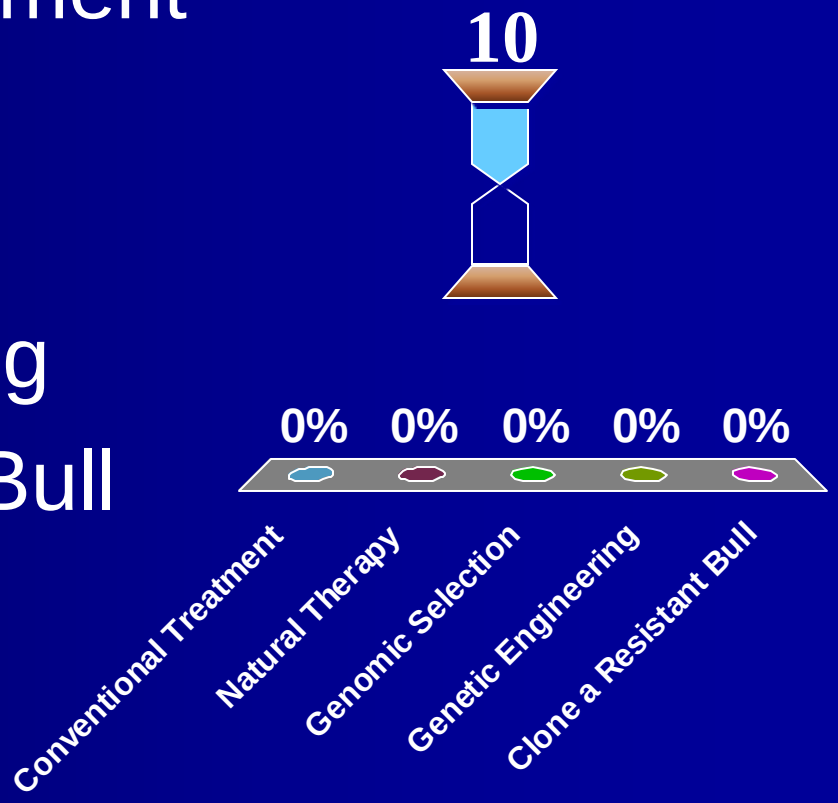
1. Conventional Treatment
2. Natural Therapy
3. Genomic Selection
4. Genetic Engineering
5. Clone a Resistant Bull



Which Animal Biotechnology would you use?

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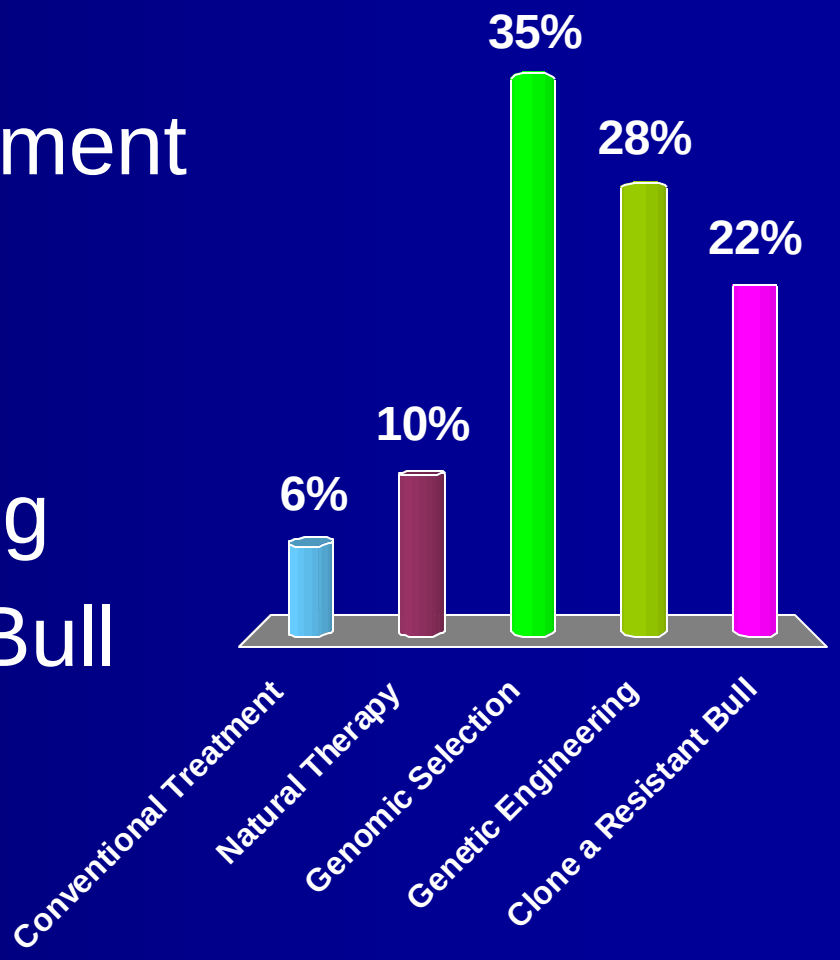
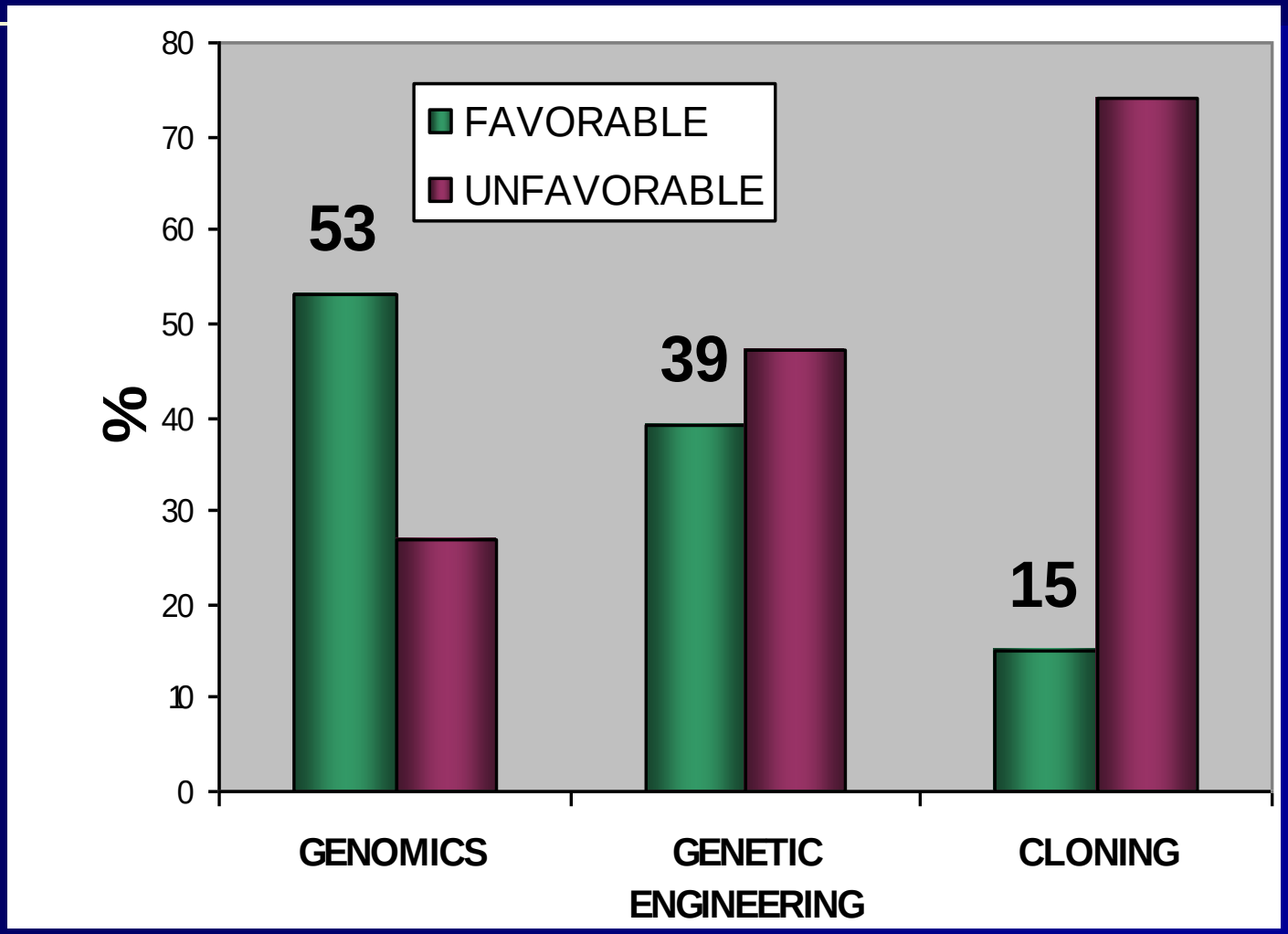


UC Davis Chancellor's Luncheon
May 2008 (n=250)

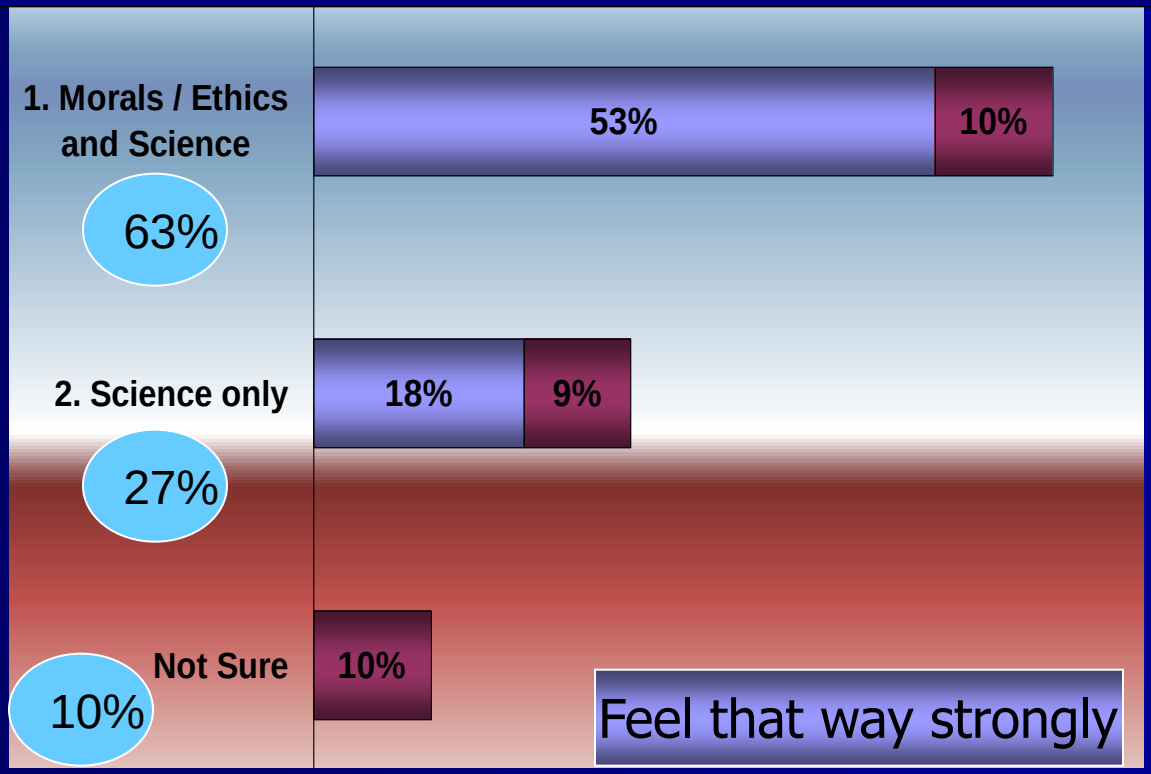
Public Attitudes Towards Specific "Animal Biotechnologies" (IFIC, 2005)



http://ific.org/research/upload/2005BiotechSurvey.pdf

1. Government regulators ***should include ethical and moral considerations***, in addition to scientific evaluation of risks and benefits, when making regulatory decisions about cloning or genetically modifying animals.

2. Though ethical and moral considerations are important, government regulators ***should consider only scientific evaluation of risks and benefits*** when making regulatory decisions about cloning and genetically modifying animals.



http://pewagbiotech.org/research/2005update/2005summary.pdf

How to incorporate social and ethical issues into regulatory decisions ?

- American consumers (75%) and scientists (70%) agree that cloning and genetic engineering of animals raise some moral and ethical issues
- However public is much less likely to approve (21-25%) of these technologies than scientists (60-68%)
- How to reach a societal consensus on ***which set of values*** will ultimately be applied to decide the acceptable uses of animal biotechnology ?

Keystone Research Center (2004) – Biotechnology and ethics: a national survey of consumers and scientists. Report to the Biotechnology Industry Organization. KRC Research, Washington DC, 29pp.

Cloning and genetic engineering of animals is an easy target for the development of morally repugnant and powerful imagery

Not milk?

Got food?

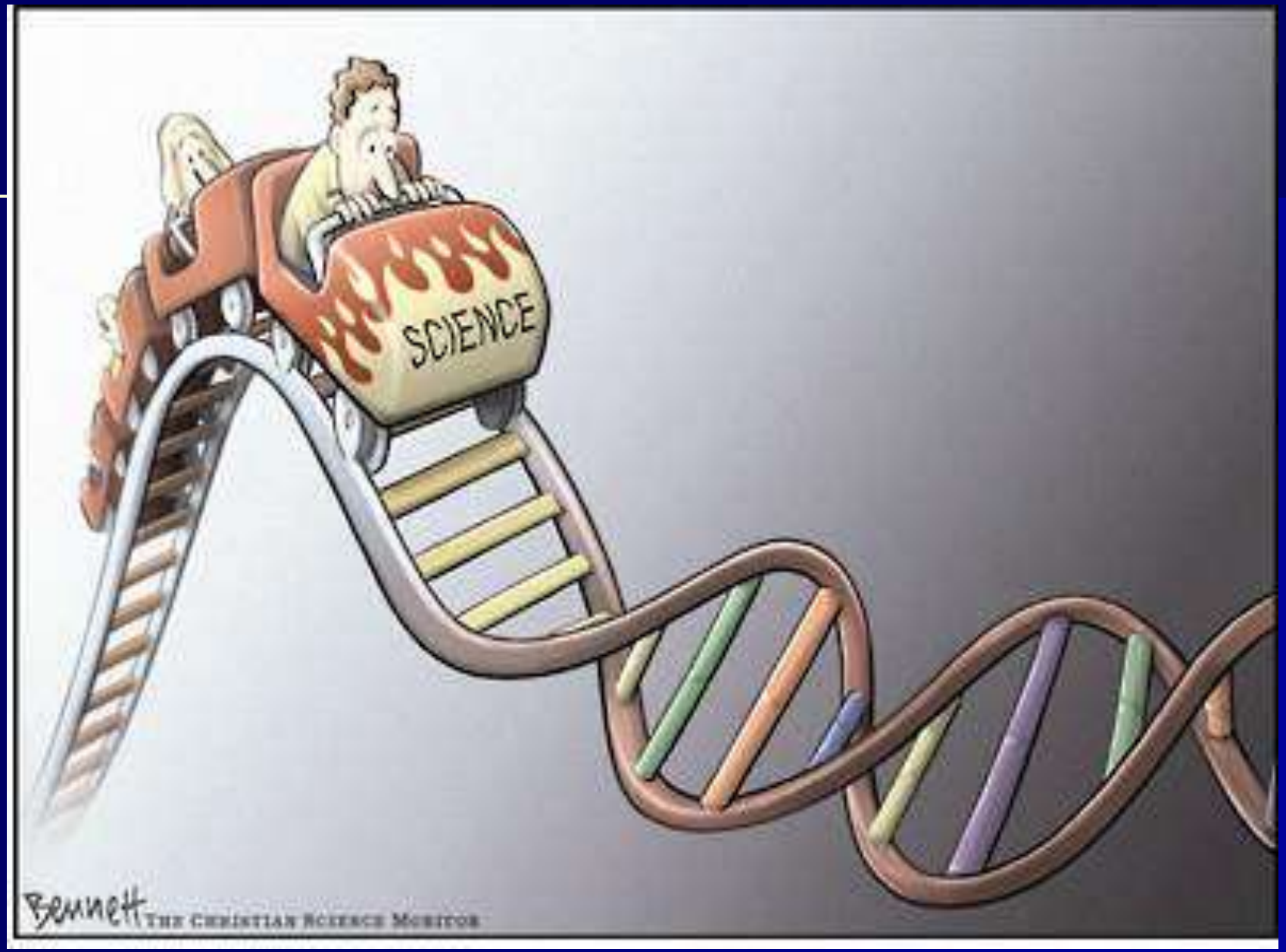
"to fail to apply the best available technologies to the solution of contemporary and future food shortages would be morally reprehensible."

Fahrenkrug et al. 2010. Precision Genetics for Complex Objectives in Animal Agriculture. J. Anim Sci. In press. doi:10.2527/jas.2010-2847

"We have recently advanced our knowledge of genetics to the point where we can manipulate life in a way never intended by nature. We must proceed with the utmost caution in the application of this new found knowledge."

LUTHER BURBANK, 1906

Creator of over 800 new plant varieties through plant breeding.


SCIENCE
Bennett
The Christian Science Monitor