TRANSLATIONAL GENOMICS: Moving animal biotechnologies from the lab to the field

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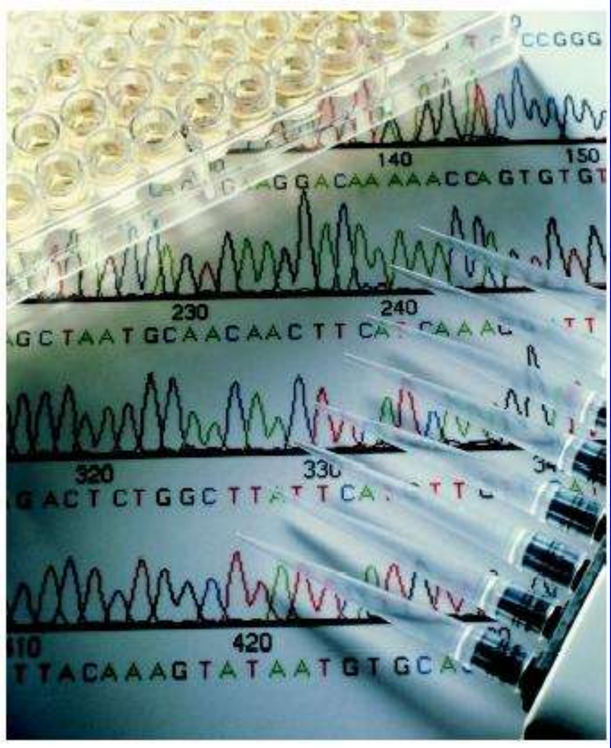


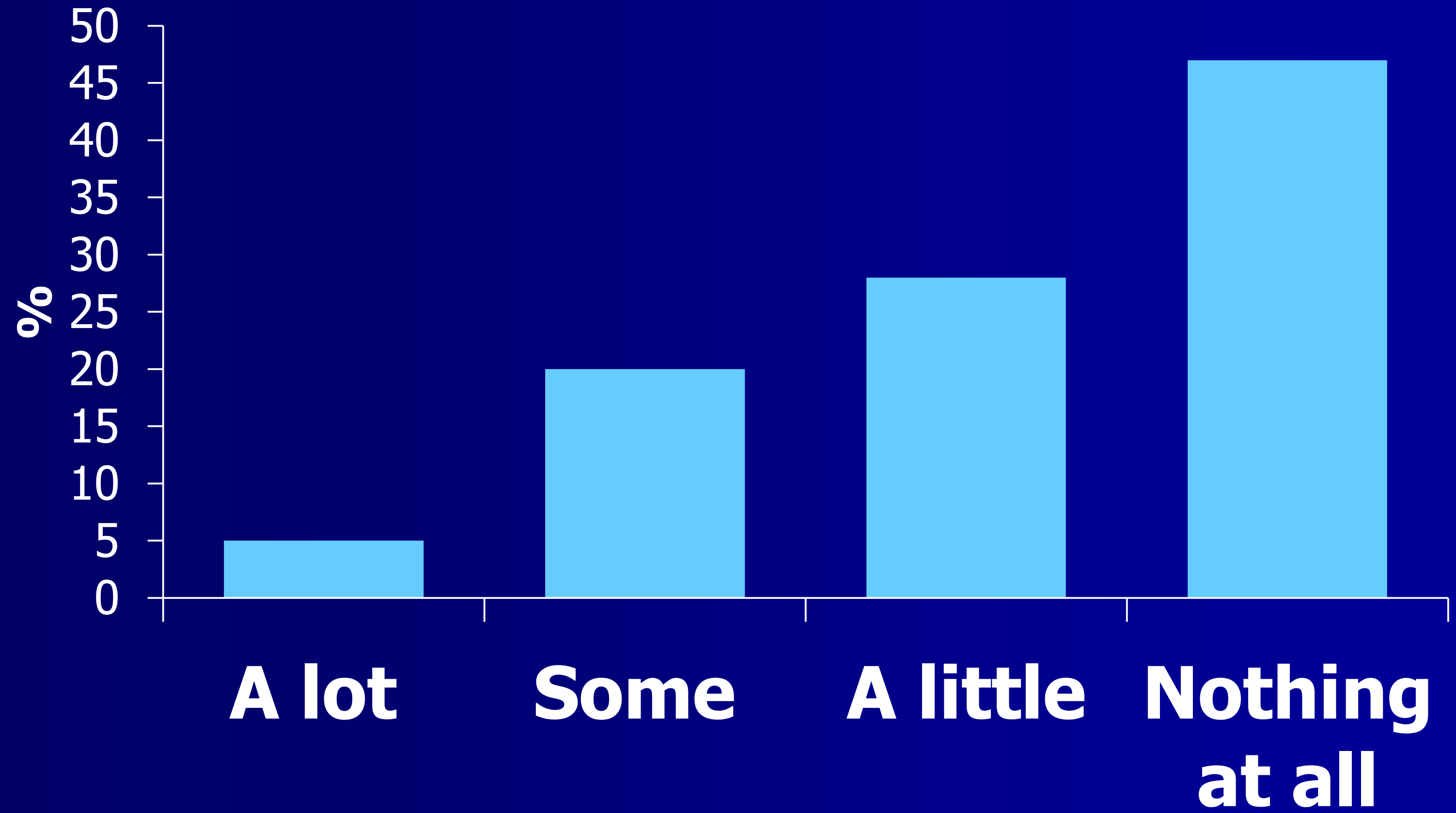
"The mission of the animal genomics and biotechnology extension program is to provide broad, science-based extension programming on the uses of animal biotechnologies in livestock production systems."

animalscience.ucdavis.edu/animalbiotech

"*Translational genomics*" is defined as the adaptation of information derived from genome technologies for animal improvement

- Rapid Uptake/Progress
  - – Genomic selection in dairy cattle
  - – Genetic defect testing
  - – DNA-based parentage testing
- Slow Uptake/Progress
  - – Genomic selection in beef cattle
- No uptake/Progress
  - – Genetic engineering for food purposes

How much have you read or heard about applying the science of biotechnology to animals? (IFIC, 2010)



http://www.foodinsight.org/Content/3843/Final%20Draft_2010%20ES%20TOPLINE%20DATA_5-26-10.pdf

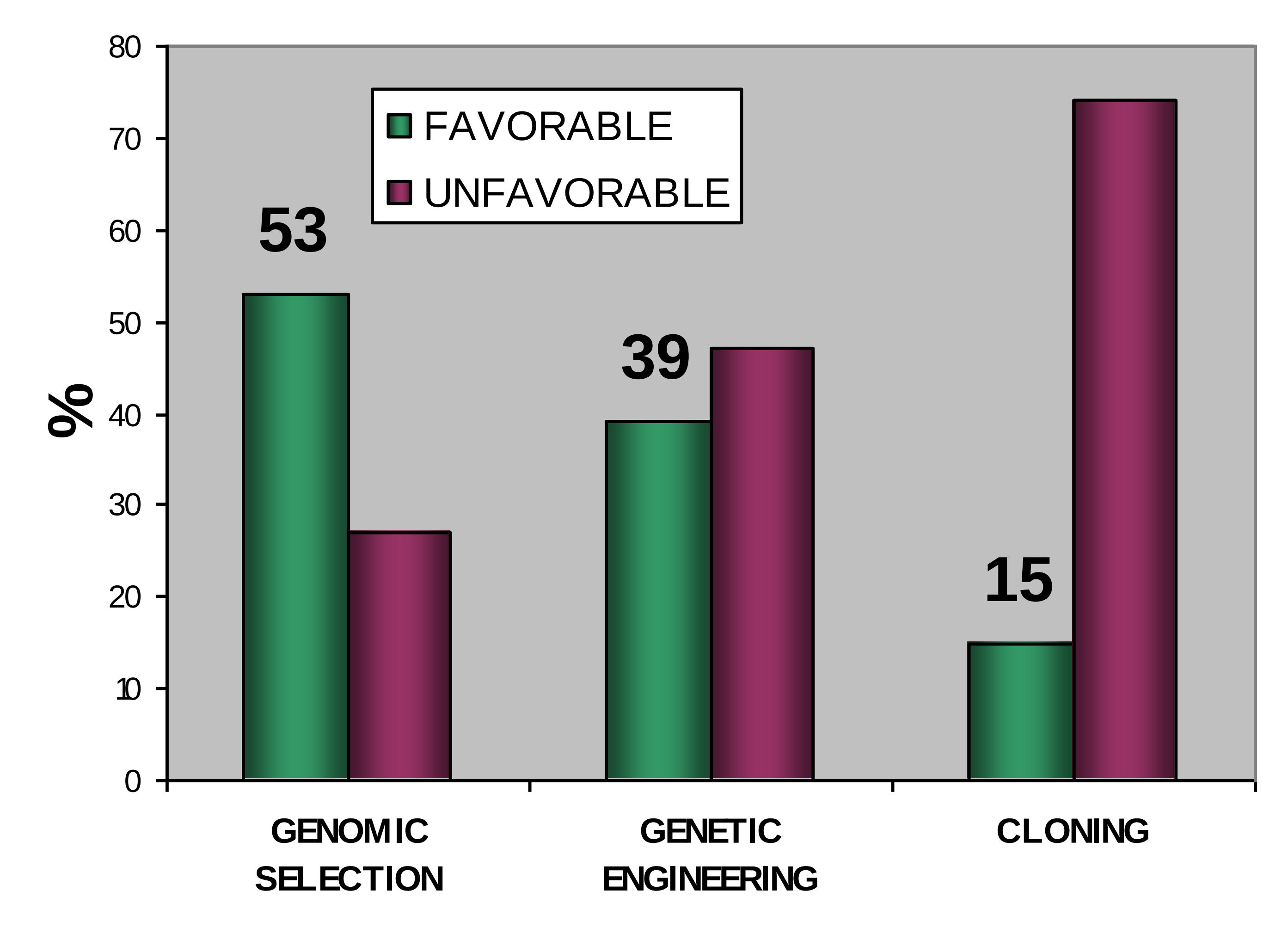
"I know it when I see it"

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.

Even though many people routinely live with genetically modified animals!

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



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

Animal biotechnologies and the breeders equation

Rate of genetic change (ΔG) =

intensity of selection X

accuracy of selection X

(√genetic variance in population /

generation interval

Genomic selection - can trace all segments of the genome with markers

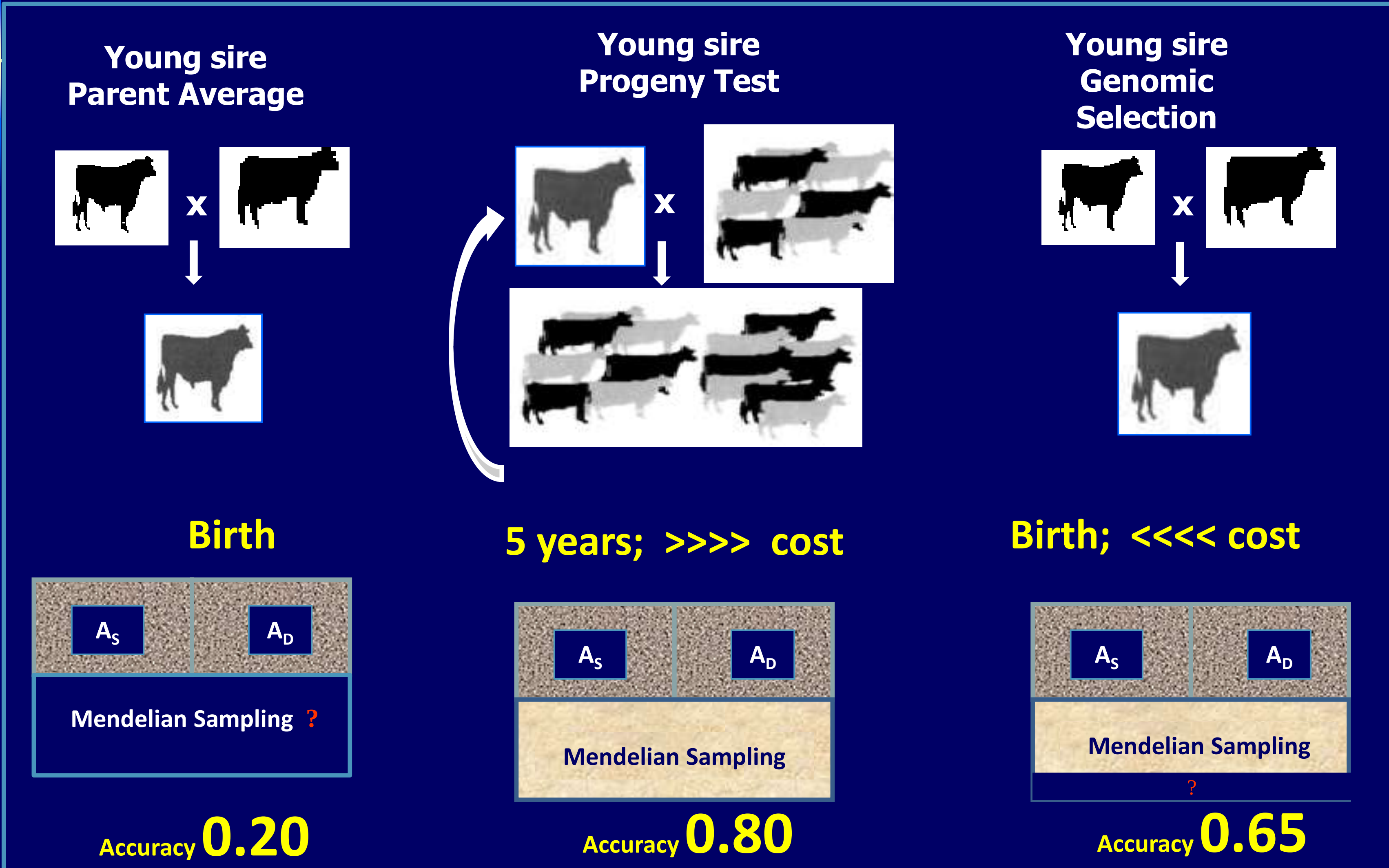
THEORY

- Population
- Phenotypes
- High density Genotypes

Training population = 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

The promise of genomic selection for the dairy industry



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

Genomic Selection and the breeders equation

Rate of genetic change (ΔG) =

intensity of selection X

accuracy of selection X

(√genetic variance in population /

generation interval

Dairy industry suited to WGS

- High use of AI
- Clear selection goal
- One breed used extensively
- 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

Another translational success story

Arthrogryposis multiplex; aka Curly Calf

- 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 RGF allele**

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

What factors promoted the rapid adoption of these animal biotechnologies?

- *"Illumina 50K bead chip released commercially January 2008, and by July the dairy industry was using it to direct its breeding approach"*
- Technically feasible
- Cost-effective or profitable
- *"The beauty of marker-assisted breeding is that it is likely to be less disconcerting to the public and regulators than transgenic or cloned animals"*

The Genome Assisted Barnyard. 2009. Nature Biotechnology 27:487.

What would the public think of Velogenetics?

- 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)

Georges and Massey (1991) *Velogenetics*, or the synergistic use of marker assisted selection and germ- line manipulation. Therieogenology 35:151-159

Velogenetics combined with genomic selection could increase rate of genetic gain 8X

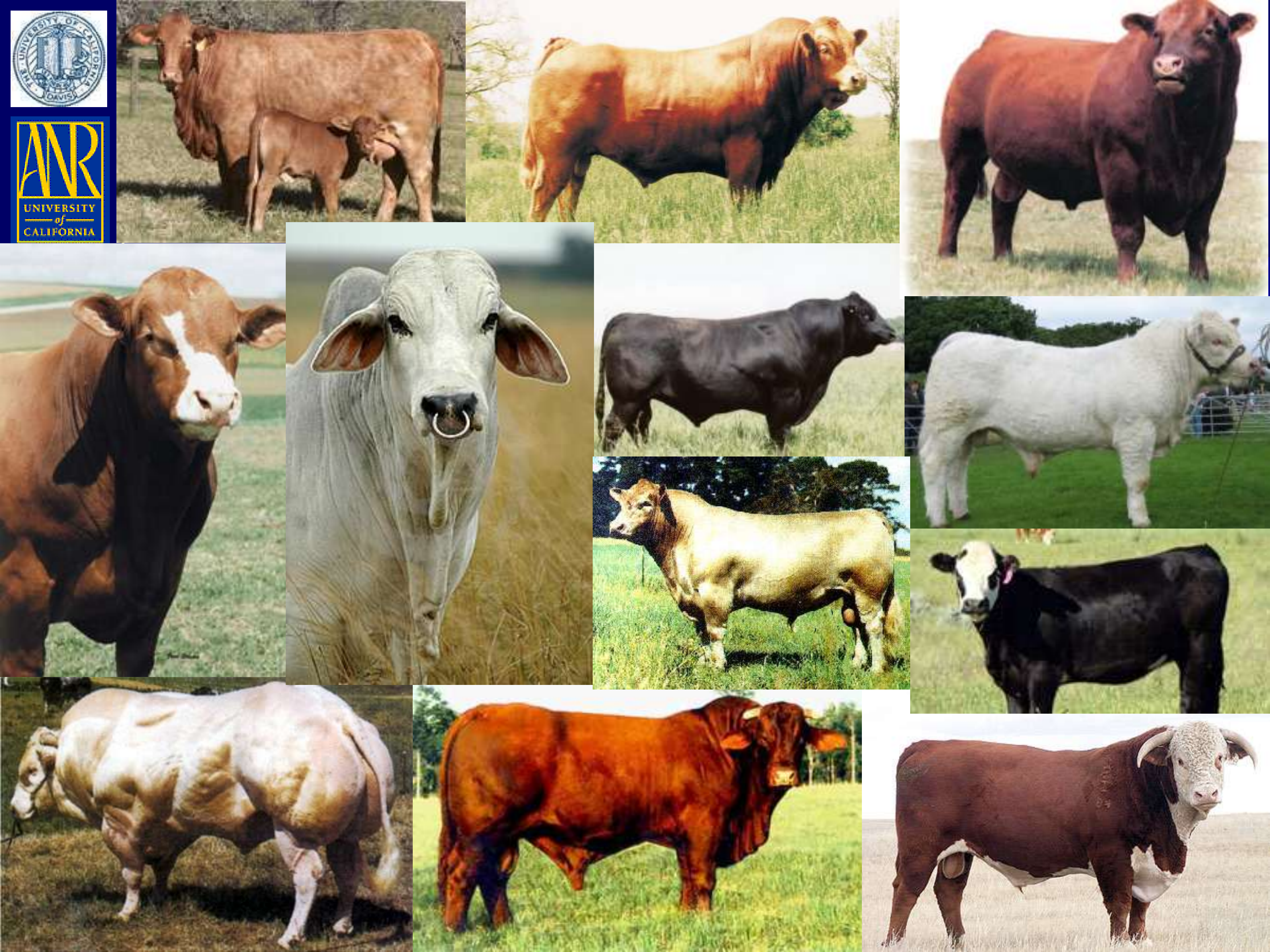
Rate of genetic gain ΔG

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

= (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



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

A perfect storm is a confluence of events that drastically aggravates a situation

Translational Questions for the Beef Cattle Industry

- ? How many phenotypic records are required in the initial training population ?
- ? How often do chromosome segment effects need to be re-estimated?
- ? How does the relationship between the training population and the selection candidate affect accuracy?
- ? Do predictions work across breeds?
- ? How many markers are needed– 50K, 800K, whole genome?
- ? What is the value generated by the increased accuracy?
- ? Does this technology change optimal breeding program design or industry structure?

The literature tells us that test accuracy (r) genetic correlation between test result and trait will increase when the following occurs:

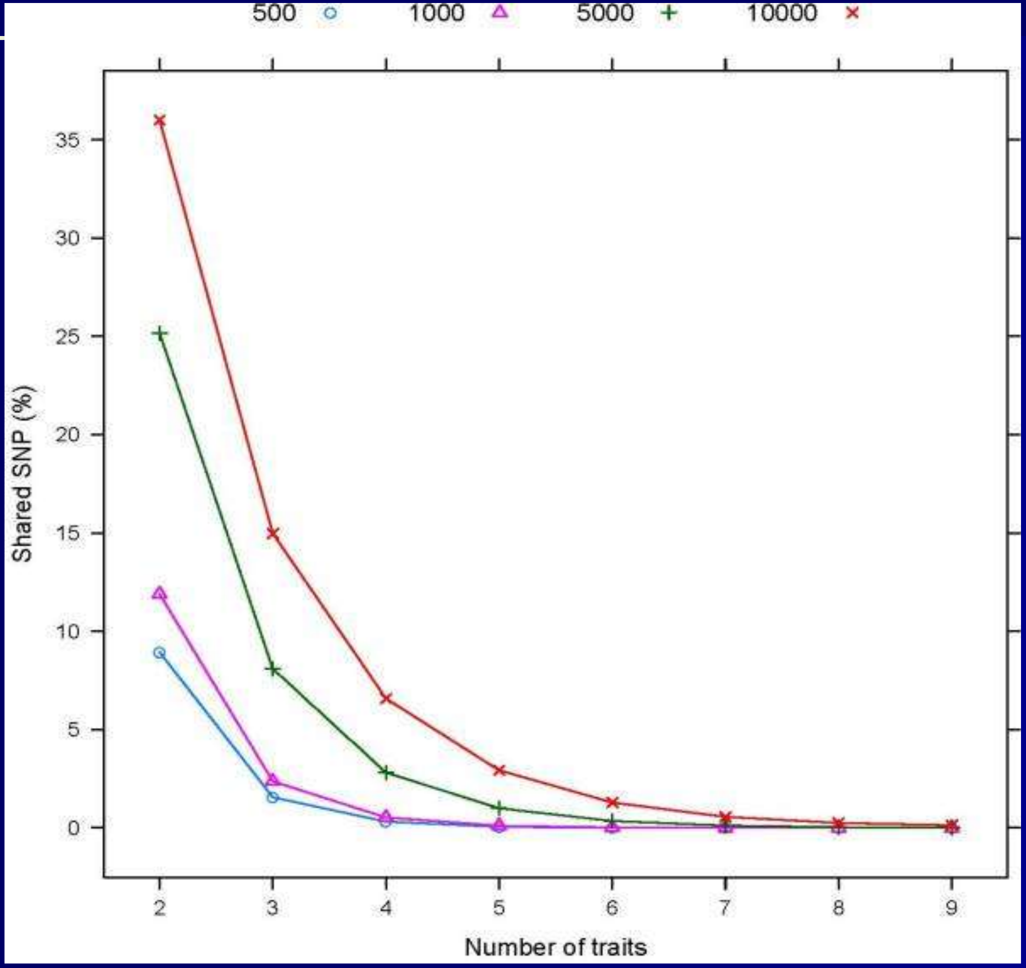
- A large number of animals and high-quality phenotypic records available for training
- High density of makers
- Heritability of the trait increases
- Small effective population size so small number of chromosome segments to track
- Small number of QTL affecting the trait so there is a marker associated with every QTL

Maybe R.A. Fisher was onto something?

If a nearly infinitesimal model is correct as seems to be the case for most quantitative traits; then large training populations will be needed to achieve high accuracy

<u>Reduced SNP panels</u>: Percentage of the highest ranked SNP that are shared between sets of traits*

for subsets including 500, 1,000, 5,000 or 10,000 SNP



* **Dairy traits included**:

1. Protein
2. Protein %
3. Survival
4. Fat %
5. Milk
6. Overall Type
7. APR (Australian Profit Rank)
8. ASI (Australian Selection Index)
9. Fat

Few SNPs were in common between the trait-specific subsets

Moser, G., M. S. Khatkar, B. J. Hayes, and H. W. Raadsma. 2010. Accuracy of direct genomic values in Holstein bulls and cows using subsets of SNP markers. Genetics Selection Evolution 42.

Other relevant interesting findings with practical implications

- Few of the “best” markers for one trait are the “best” for a second trait and fewer still more than two
- Prediction equations derived in one breed do not predict accurate MBVs when applied to other breeds
- Combining breeds into one large multi-breed reference population gives reasonable accuracies in purebreds
- To find markers that are in LD with QTL across diverged breeds, such as Holstein, Jersey, and Angus, will require high density SNPs (>300,000 markers)
- If markers are picking up family relationships (linkage), then the accuracy of marker-based selection will decay over generations within breed

Given that background what beef products are in use and do they conform with literature predictions?

GeneSTAR
SureTRAK
SireTRACE
GeneSTAR
Pfizer
Pfizer Animal Genetics

igenity

ImmGen.

GENETICVISIONS

genmark

BIOGENETIC SERVICES, INC.

GENESEEK
Molecular Solutions for Breeding and Genetics

ANGUSURE

GENAISSANCE PHARMACEUTICALS

MMI GENOMICS, INC.
BREED TRU
DNA VERIFIED

METAMORPHIX, INC.

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 Circumference**

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

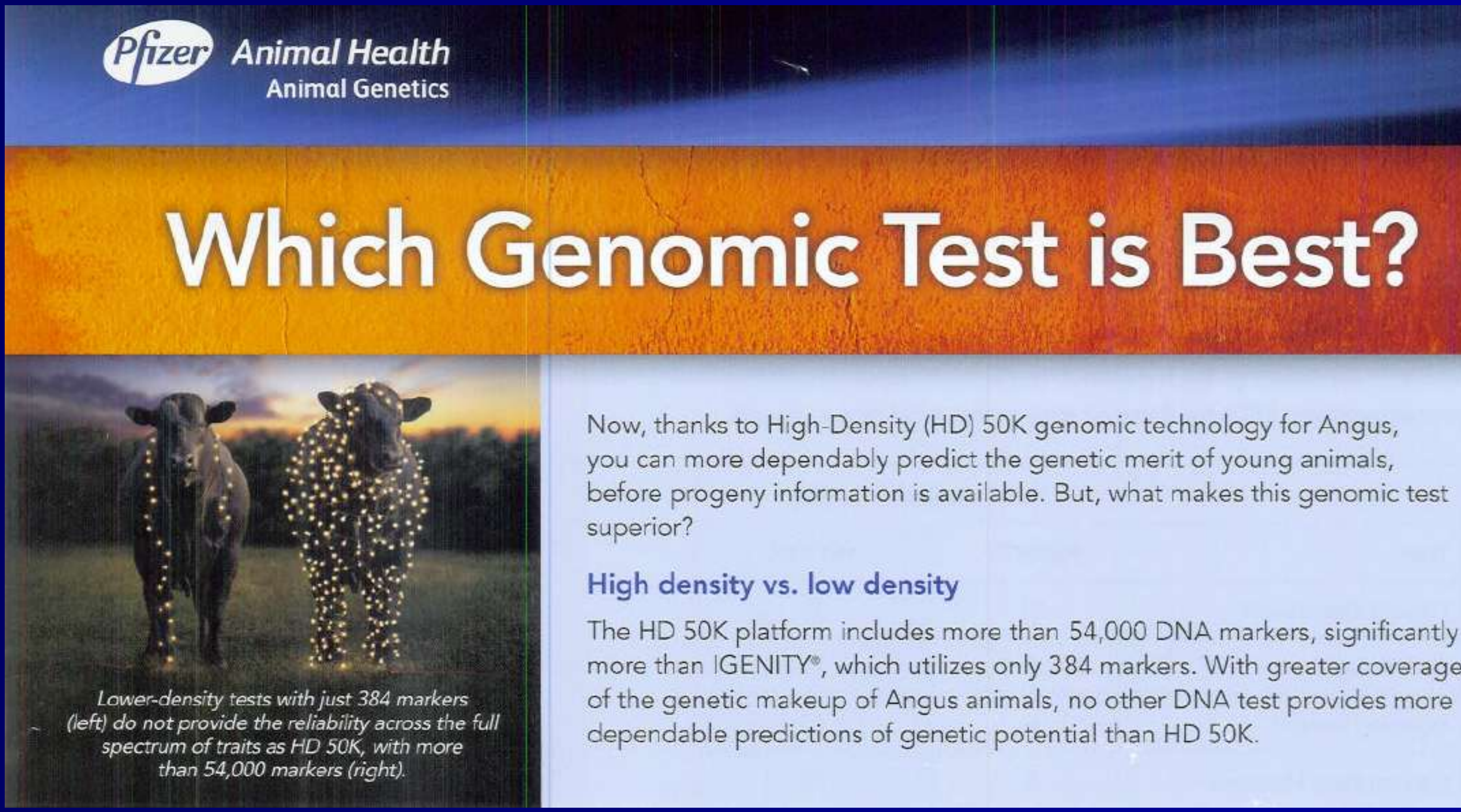
50K SNP chip assays 50,000 SNPs spread throughout genome

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)

So the question I get asked a lot is:



Genetic correlations for National Cattle Evaluation traits in Angus by company

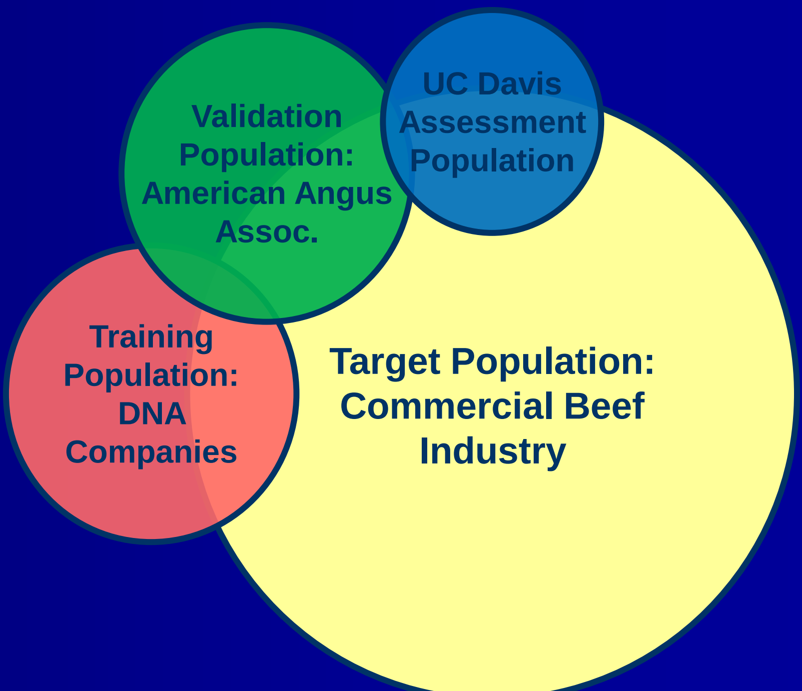
	384 SNP	50K SNP
	Igenity	Pfizer
Calving Ease Direct	.47	.33
Birth Weight	.57	.51
Weaning Weight	.45	.52
Yearling Weight	.34	.64
Milk	.24	.32
Carcass Marbling	.65	.57
Carcass Rib	.58	.60
Carcass Fat	.50	.56
Carcass Weight	.54	.48
Dry Matter Intake (component of RADG)	.45	.65
Docility	.47	n/a

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

Independent Assessment of Commercial Tests for Beef Cattle Production Traits

The objective of this study was to estimate the genetic correlation between MBVs and target traits based on ranch genetic evaluations of herd bulls sourced from the Angus seedstock sector.

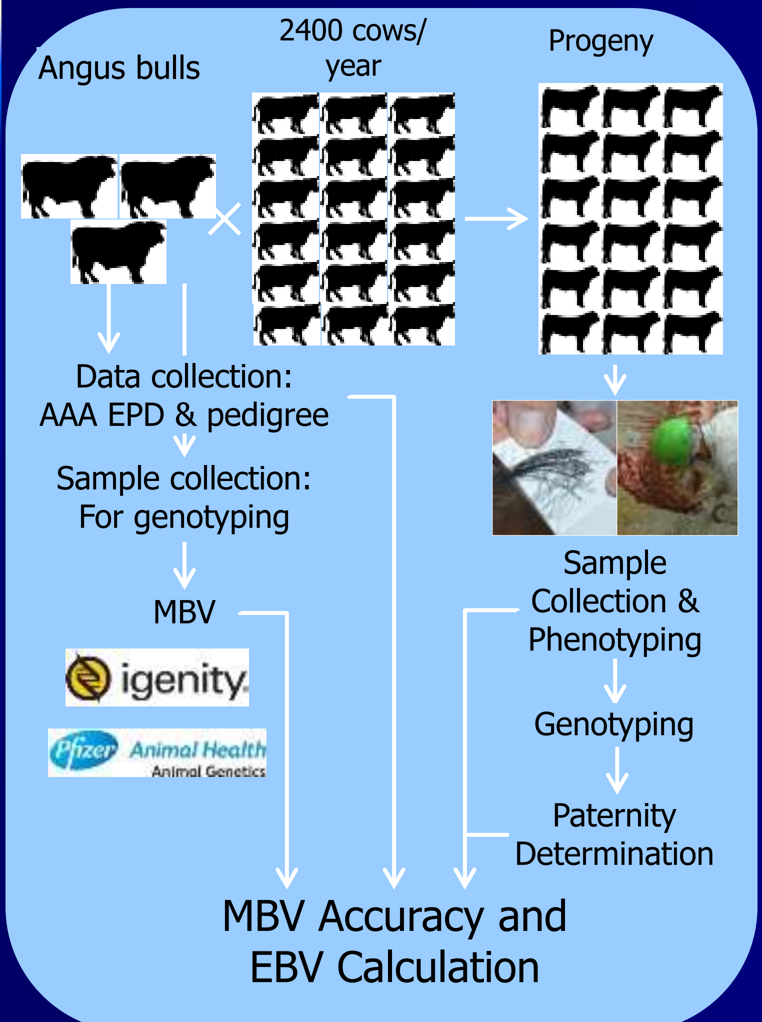
	Trait				
	WW	ADG	HCW	RE	MS
# bulls	114	114	114	114	114
# progeny	1734	341	455	455	455
Avg # progeny per bull	60	12	16	16	16



Weber, KL, and A.L. Van Eenennaam. American Society of Animal Science Late Breaking Abstract, July 11, 2011, New Orleans, LA

UC Davis Commercial Ranch Project

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.



Traits:

- weaning weight (WW)
- average daily gain (ADG)
- hot carcass weight (HCW)
- ribeye area (RE)
- marbling score (MS)

By 2013, 7000 progeny records of over 125 bulls will have been collected

	Trait				
	WW	ADG	HCW	RE	MS
Phenotype mean (SD)	226± 35kg	1.1± 0.2kg/day	333± 34kg	80±7 cm²	5.8± 1.0
Heritability (est.)	0.22	0.17	0.30	0.39	0.44
Avg BIF accuracy of original AAA EPD	0.23		0.18	0.25	0.22

Methods: Estimating breeding values and genetic correlation (r) between MBV and ranch EBVs of herd bulls sourced from the Angus seedstock sector.

- Accuracy of MBV (or MVP) = the genetic correlation between the MBV (or MVP) and the same trait in the assessment population, estimated in a multivariate animal model (Kachman, 2008).

$$y = Xb + Za + e$$

  - Fixed effects for phenotypes included contemporary group, sex, and for weaning weight, age of dam and pre-adjustment to 205-days of age.
  - A maternal model was used in the weaning weight analysis.
  - Average daily gain was calculated as the rate of gain per day between feedlot in-weight and final weight (estimated as hot carcass weight/0.63).
  - Ranch EBV were calculated using a univariate animal model, otherwise the same as the multivariate analyses

Independent assessment of the accuracy (r) of Angus- and across-breed genomic breeding values in Angus bulls from three Northern California commercial ranches

Weber, KL, et al. 2011. Journal of Animal Science. *In preparation*

Training population	MBV	Number Bulls*	Genetic correlation (r) with Trait				
			WW	ADG	CW	MS	RE
Multi-breed	$MARC_{GPE}$	114	-0.04 (0.15)		0.30 (0.21)	0.33 (0.20)	0.23 (0.20)
	2K Bull Project	114	0.17 (0.15)			0.36 (0.21)	0.16 (0.21)
Angus	$2KBP_{ANGUS\ ONLY}$	114	0.15 (0.15)		0.17 (0.19)	0.66 (0.14)	0.18 (0.19)
	$MBV_{Igenity}$	AAA	.45		.54	.65	.58
	$MBV_{Igenity}$	29	0.11 (0.22)	-0.01 (0.42)	0.33 (0.27)	0.61 (0.19)	0.34 (0.24)
	MVP_{Pfizer}	AAA	.52		.48	.57	.60
	MVP_{Pfizer}	29	0.51 (0.17)	0.10 (0.39)	0.08 (0.28)	0.71 (0.17)	0.56 (0.21)
	MU (Mizzou)	105	0.21 (0.15)		0.40 (0.19)	0.88 (0.09)	0.40 (0.18)
Hereford							
	$2KBP_{HH}$	114	0.09 (0.15)			-0.07 (0.24)	0.24 (0.21)

* Number of Bulls that were included in assessment population

$MARC_{GPE}$=trained on USMARC GPE Cycle VII continuously-sampled phenotypes

2K Bull project=trained on 2000 Bull deregressed EBV

$2KBP_{ANGUS\ ONLY}$= trained on 2KBP Angus only bulls (N=402) deregressed breeding values

$MBV_{Igenity}$ = IGENITY results

MVP_{Pfizer} = Pfizer results

MU (Missou) = University of Missouri, Columbia Angus prediction equation

$2KBP_{HH}$=trained on 2000 Bull Hereford deregressed breeding values

Genetic engineering and the breeders equation

ΔG = ***intensity of selection X***

accuracy of selection X

(√genetic variance in population /

generation interval)

56% of Americans oppose scientific research into the genetic modification of animals

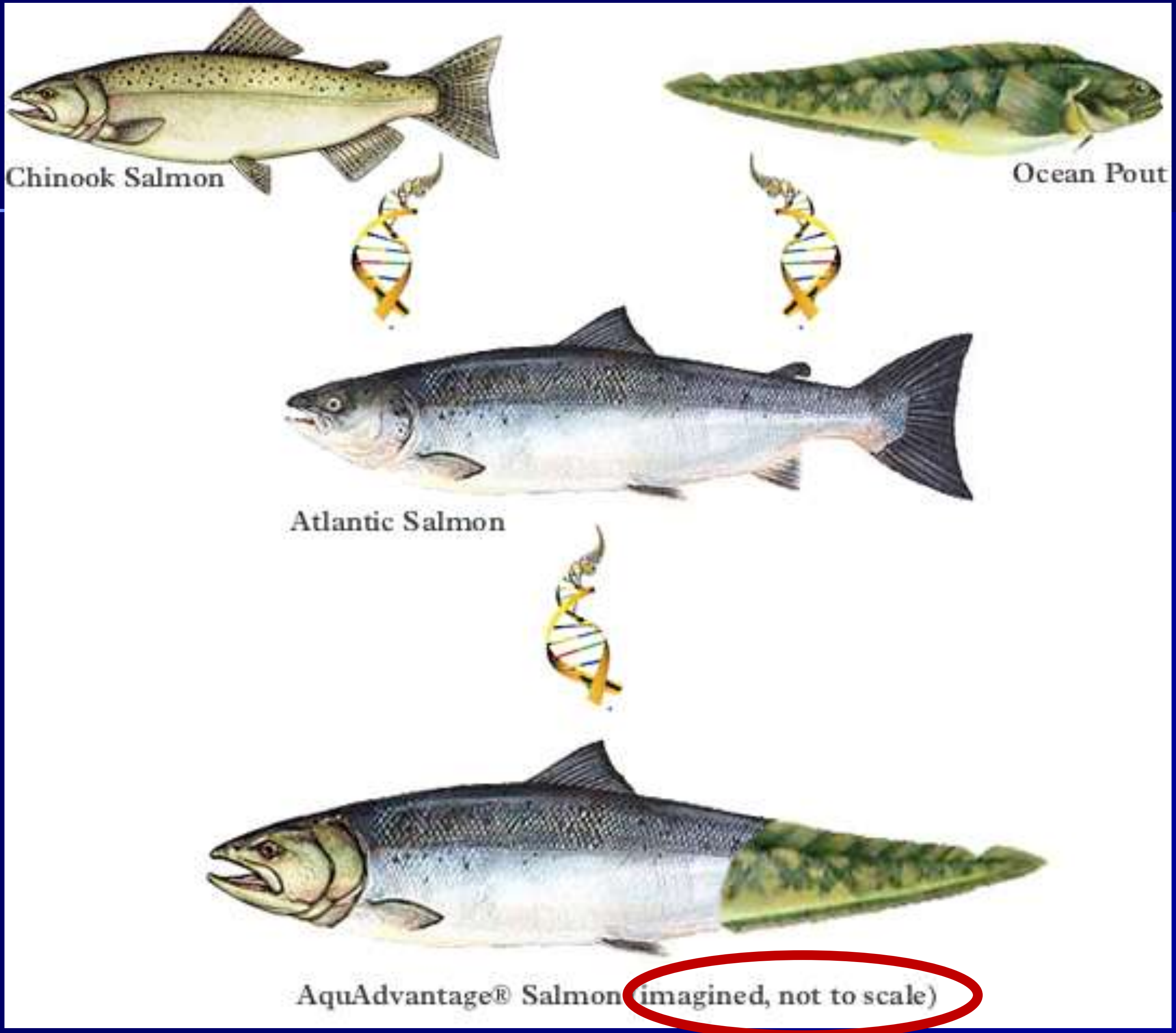
http://pewagbiotech.org/research/2005update/2005summary.pdf

The genetic modification of animals is an easy target for the development of morally repugnant and powerful imagery

Even though the phenotype of most GE animals is rather unremarkable……

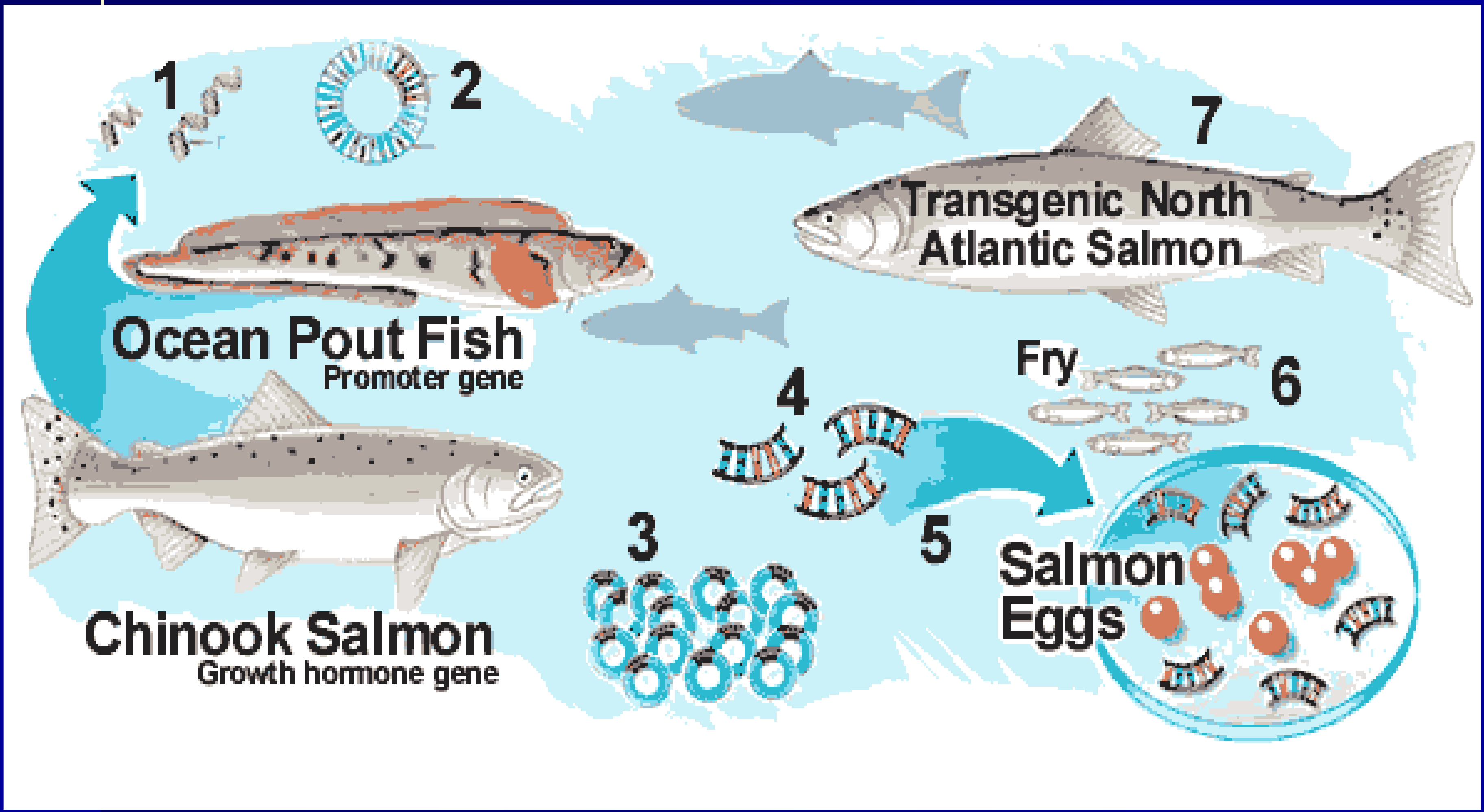
Let us consider the case of the AquAdvantage salmon

Retrieved from “AquAdvantage” image search on web

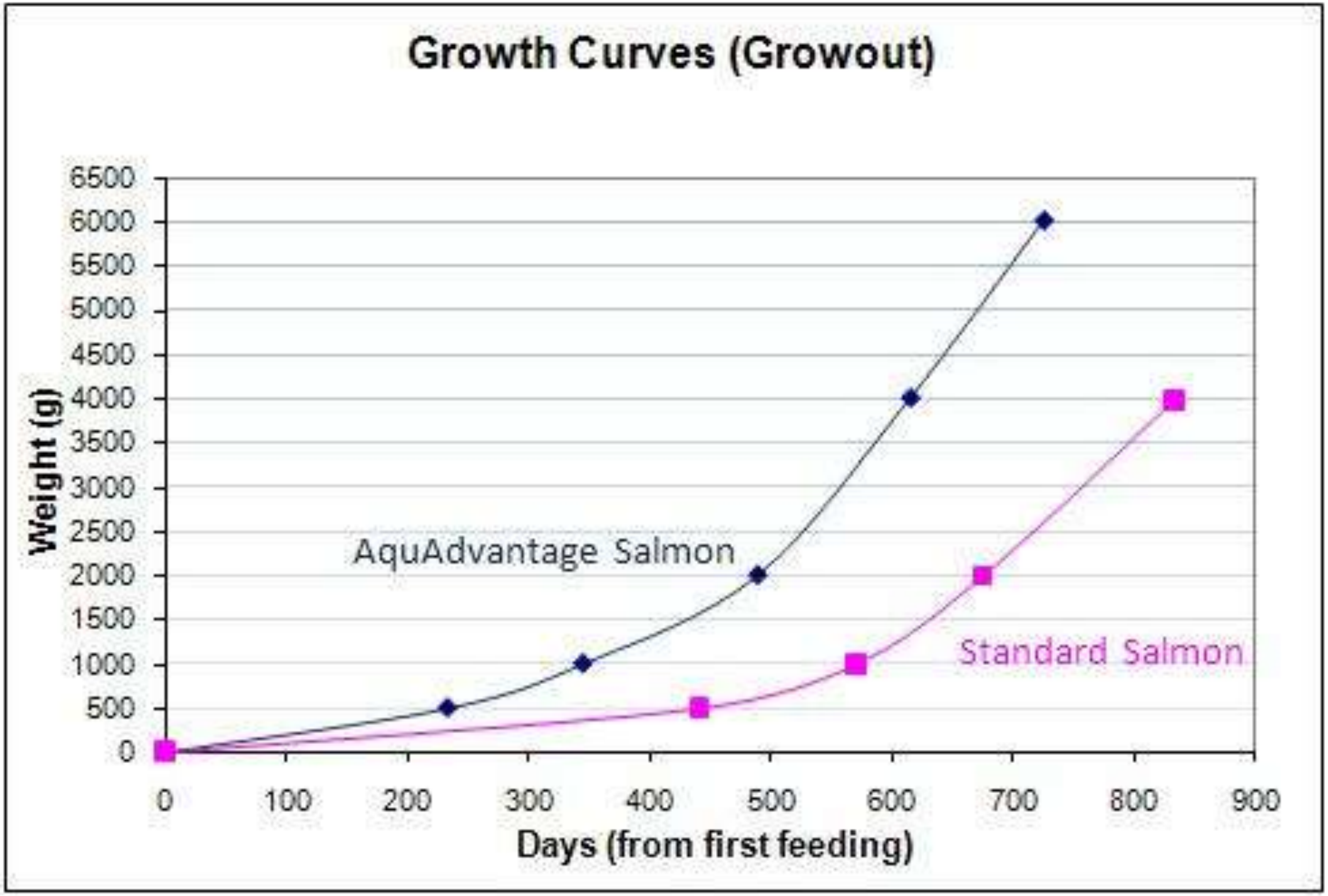


Retrieved from "AquAdvantage" image search on web
Frankenfish

What is the AquAdvantage salmon?



Fish reach adult size in 16 to 18 months instead of 30 months



A formal application for a New Animal Drug Application with an intent to commercialize AquAdvantage salmon was made on September 14, 1995. FDA public Veterinary Medicine Advisory Committee (VMAC) Meeting was held September 19-20th, 2010

SCIENCE

Frankenfood, Coming Soon to a Store Near You?

Published September 20, 2010 | FoxNews.com

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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.

"There is little benefit to society if attempts to increase public participation in the regulatory process are used as an opportunity to vilify technology."

Transgenic salmon: a final leap to the grocery shelf?

Alison L Van Eenennaam & William M Muir

Nature Biotechnology (2011) **29**: 706–710.

Despite being caught up in regulatory proceedings for 15 years or more, AquAdvantage salmon, the first animal genetically engineered (GE) for food purposes, continues to raise concerns. Are any of these concerns scientifically justified?

The tortuous passage of AquAdvantage salmon through the US regulatory system provides a stark reminder of the adage that sometimes it is good not to be first. A fast-growing transgenic fish containing a gene encoding Chinook salmon growth hormone under the control of an antifreeze protein promoter and terminator from ocean pout, AquAdvantage salmon has been subjected to one of the most prolonged, if not exhaustive, regulatory assessments in history. This process culminated last September with a meeting of the Veterinary Medicine Advisory Committee (VMAC) as well as a public hearing, together with the release of a comprehensive health and safety briefing and an environmental assessment package on the transgenic animal developed by AquaBounty Technologies of Waltham, Massachusetts. Despite VMAC's determination


AquaBounty Technologies

Extant GE livestock applications

ENVIRONMENTAL	Species	Gene	Approach
Decreased P in manure	Swine	Phytase	Transgene overexpression
DISEASE RESISTANCE			
Mastitis resistance	Cattle	Lysostaphin	Transgene expression
BSE resistance	Goat, Cattle	Prion	RNAi transgene; knockout
Visna virus resistance	Sheep	Visna virus envelope gene	Transgene expression
Mastitis resistance	Goats	Lysozyme	Transgene expression
GCH virus resistance	Grass Carp	Lactoferrin	Transgene expression
Bacterial resistance	Channel Catfish	Cecropin B gene	Transgene expression
PRODUCT QUALITY			
Increased ω-3 fatty acids in meat	Swine	n-3 fatty acid desaturase	Clone/Transgene expression
Increase cheese yield from milk	Cattle	β-casein, κ-casein	Clone/Transgene expression
PRODUCTIVITY			
Enhanced growth rate	Many fish species	Growth Hormone	Transgene expression
Enhanced milk production	Swine	α-lactalbumin	Transgene expression
Enhanced growth rate	Swine	Growth hormone	Transgene expression
Enhanced growth rate	Swine	Insulin-like-growth factor	Transgene expression

Fahrenkrug et al. 2010. Precision Genetics for Complex Objectives in Animal Agriculture. J. Anim Sci. 88: 2530-2539

Proportional increase in world head of livestock 1961-2004; data from FAO (2005)

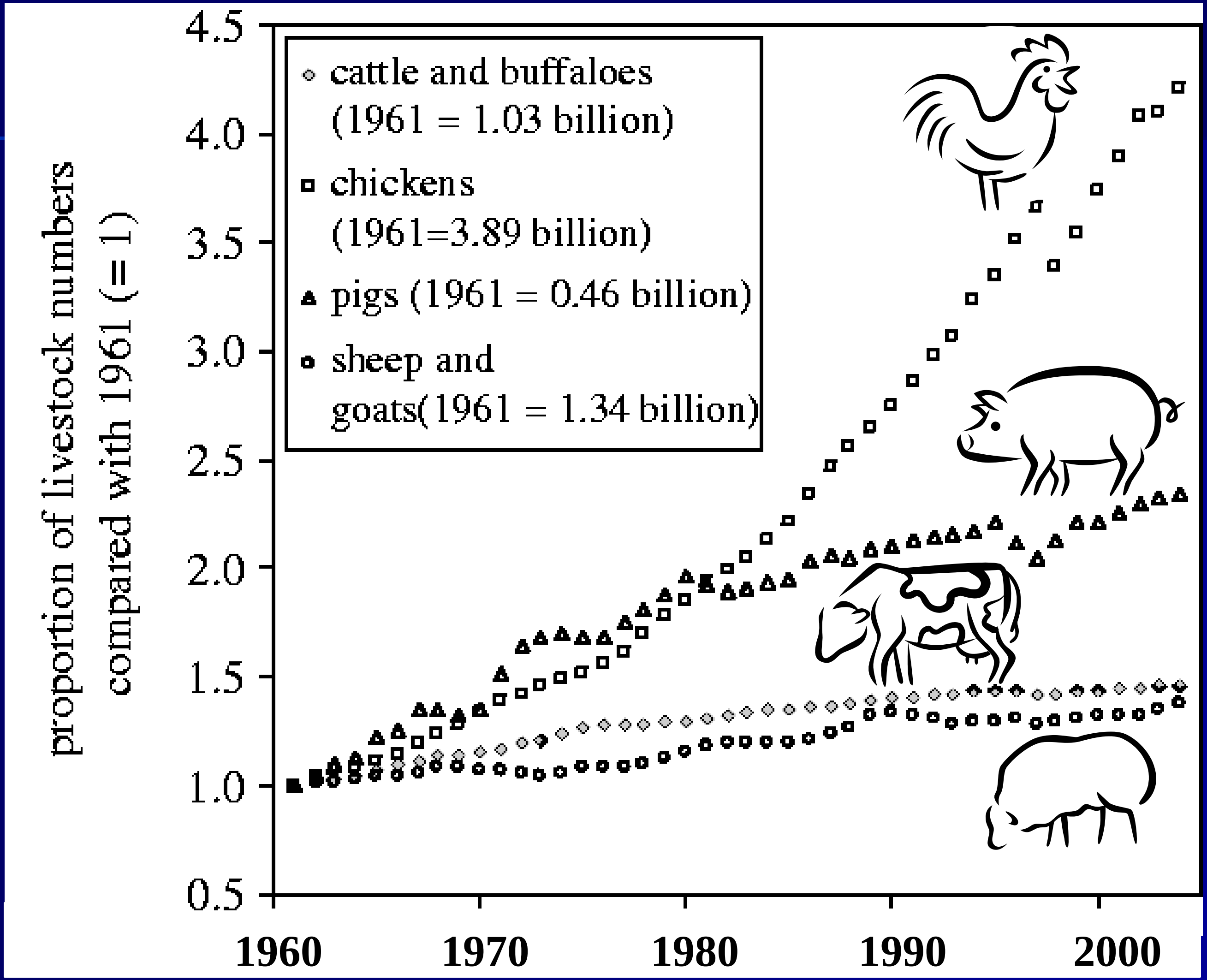

Figure based on Pretty, J. (2008) Agricultural sustainability: concepts, principles and evidence. Philosophical Transactions of the Royal Society B-Biological Sciences 363:447-465.

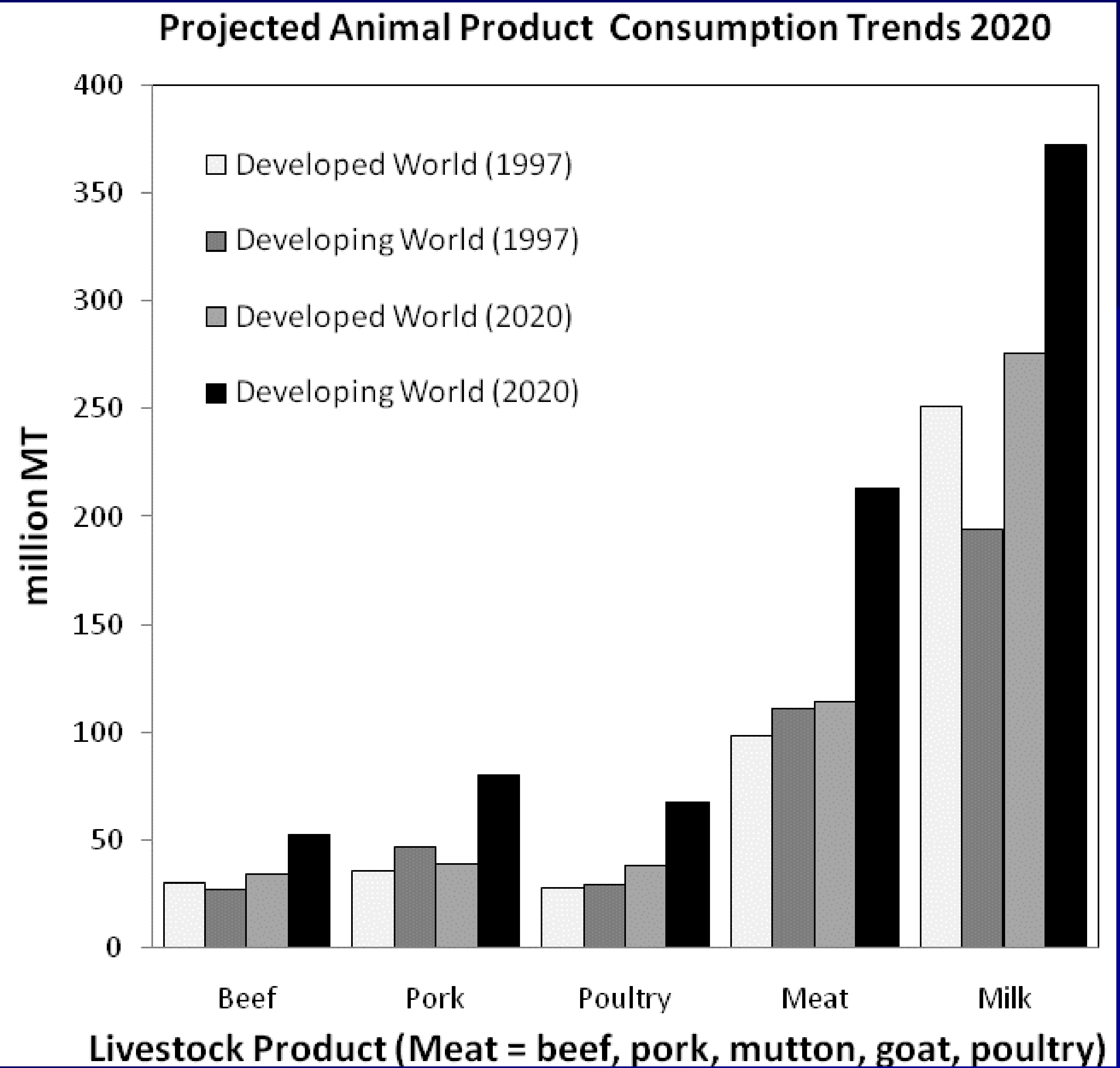

Figure from Delgado, C. L. 2003. Rising consumption of meat and milk in developing countries has created a new food revolution. Journal of Nutrition 133:3907S-3910S.

"Would there be general acceptance of transgenic technology if it could be applied to engineering resistance to influenza in poultry and therefore lessen the risk of an influenza epidemic, such as the one in 1918 that killed more than 20 million people?"

Clark,J. & Whitelaw,B. 2003. A future for transgenic livestock. Nature Reviews Genetics 4, 825-833

Sustainable, disease-resistant genetically modified animals

Suppression of Avian Influenza Transmission in Genetically Modified Chickens

Jon Lyall,[1] Richard M. Irvine,[2] Adrian Sherman,[3] Trevelyan J. McKinley,[1] Alejand
Auriol Purdie,[3*] Linzy Outtrim,[2] Ian H. Brown,[2] Genevieve Rolleston-Smith,[3]
Helen Sang,[3]† Laurence Tiley[1]†‡

Infection of chickens with avian influenza virus poses a global threat to both poultry production and human health that is not adequately controlled by vaccination or by biosecurity measures. A novel alternative strategy is to develop chickens that are genetically resistant to infection. We generated transgenic chickens expressing a short-hairpin RNA designed to function as a decoy that inhibits and blocks influenza virus polymerase and hence interferes with virus propagation. Susceptibility to primary challenge with highly pathogenic avian influenza virus and onward transmission dynamics were determined. Although the transgenic birds succumbed to the initial experimental challenge, onward transmission to both transgenic and nontransgenic birds was prevented.

The diversity of avian influenza viruses (AIVs) and their propensity for inter-species transmission make them a global

mediate host species that amplify and diversify virus populations, notably domestic chickens, ducks, and pigs (*1*). Although control of AIV in-

inhibiting influenza viral polymerase activity (*6*).

An RNA expression cassette (Fig. 1A) was designed to use a chicken U6 promoter (*7*) to express the short hairpin RNA molecule, decoy 5 (D5, Fig. 1B) (*8*). This decoy contains the conserved 3′- and 5′-terminal sequences of influenza virus genome segments that encompass the complementary RNA (cRNA) binding site for

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*Present address: Faculty of Veterinary Science, University of Sydney, NSW 2567, Australia.

Lyall et al. 2011. Suppression of Avian Influenza Transmission in Genetically Modified Chickens. Science. 331:223-226

Envisioned GE livestock applications

ENVISIONED APPICATIONS	Species	Proposed Approach
Suppressing infectious pathogens (e.g. Avian flu resistance)	Various	RNAi (Lentivirus)
Coronavirus-resistance	Swine	RNAi /Knockout
Low lactose milk	Cattle	Transgene expression
Low lactose milk	Cattle	RNAi /Knockout
Increased ovulation rate	Sheep	RNAi /Knockout
High omega-3 fatty acid milk	Cattle	Transgene expression
Resistance to Brucellosis	Cattle	Transgene expression
Decreased P in manure	Poultry	Transgene expression
Increased lean-muscle growth	Cattle	RNAi /Knockout
Increased post-natal growth	Various	RNAi /Knockout
Enhanced mammary gland development	Various	RNAi /Knockout

Fahrenkrug et al. 2010. Precision Genetics for Complex Objectives in Animal Agriculture. J. Animal Sci. 88: 2530-2539


HARDIN
"We've considered every potential risk except the risks of avoiding all risks."

Cloning and the breeders equation

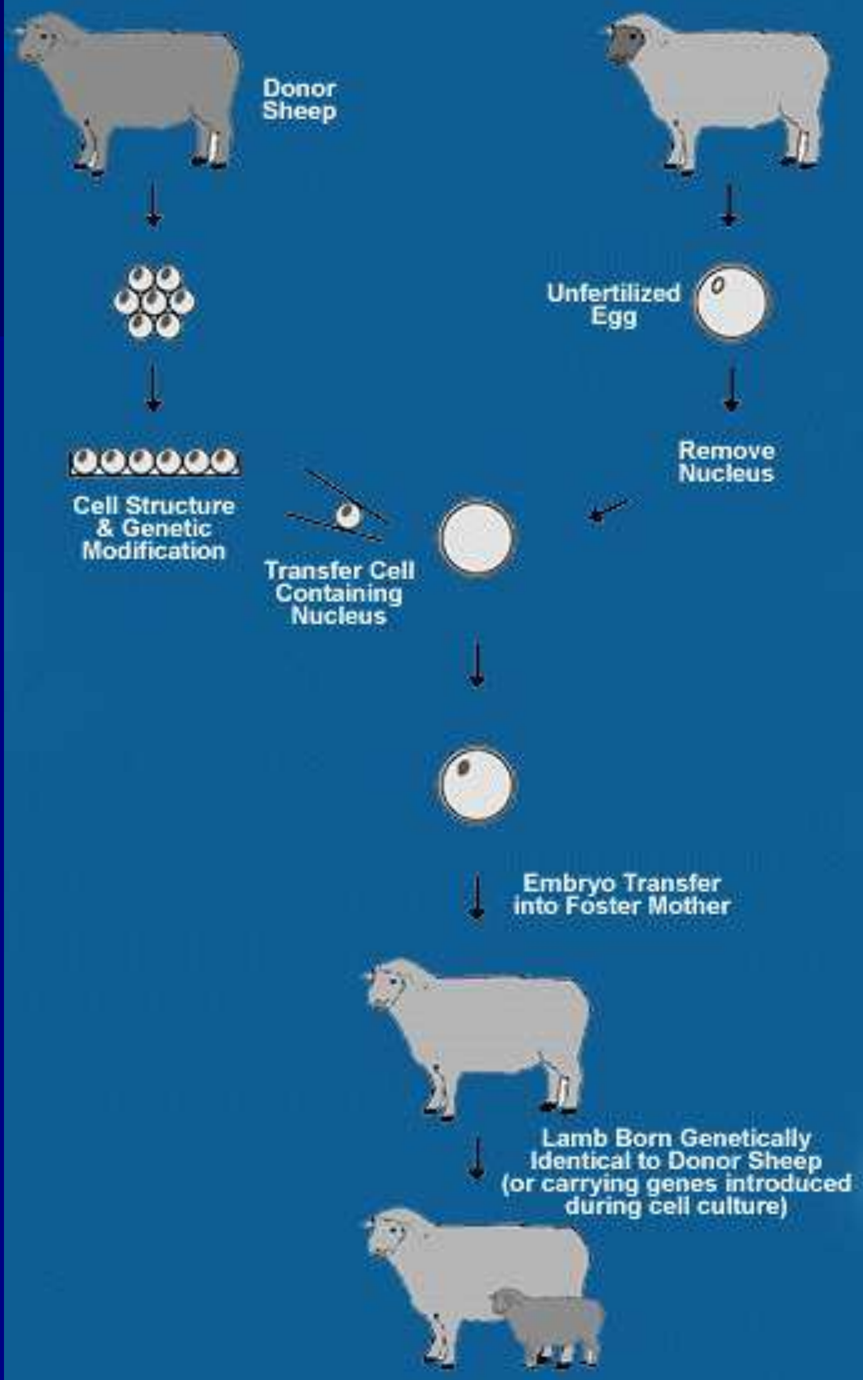
ΔG = ***intensity of selection X***

accuracy of selection X

(√genetic variance in population /

generation interval)

Dolly (1996), the first adult somatic cell nuclear transfer (SCNT) clone



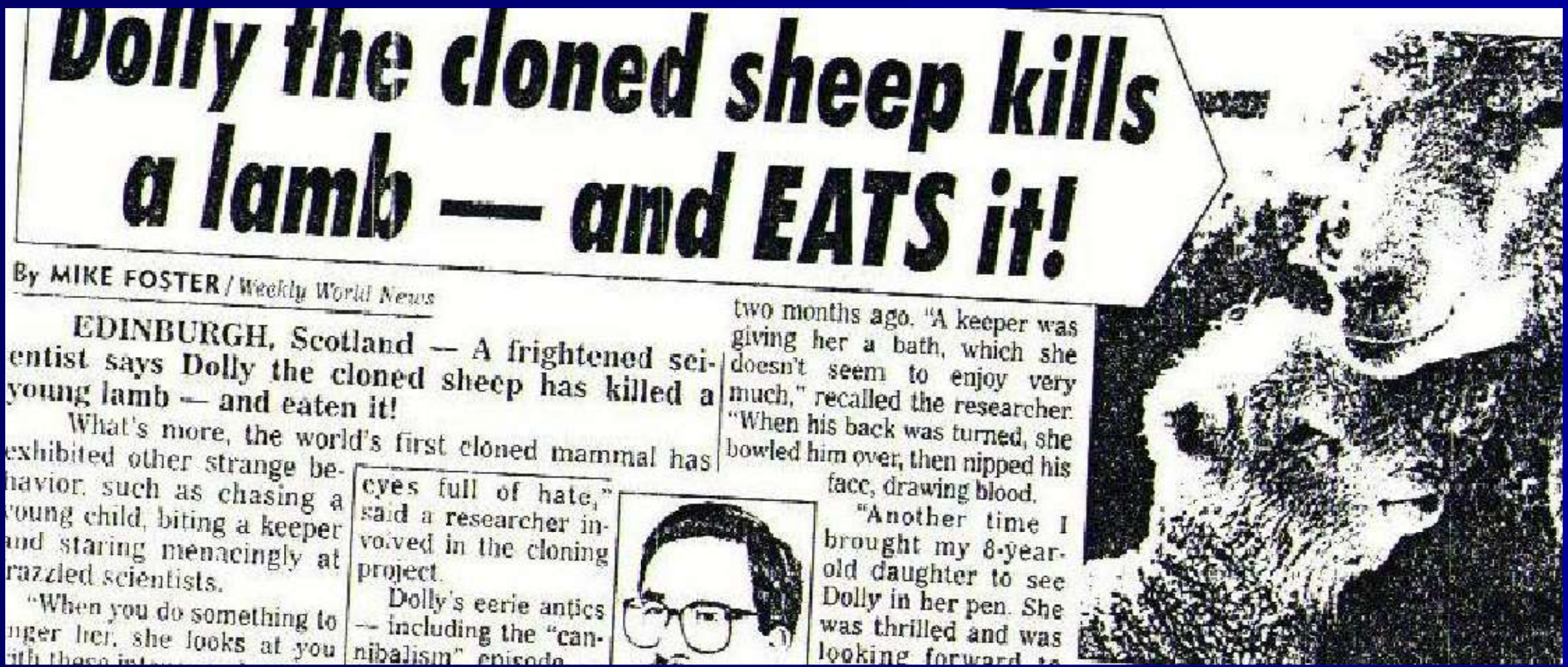
Who's Buying? Elite breeding and show stock

Regancrest Emory Derry died unexpectedly.

Full Flush
Unable to supply market demand for his semen

Dolly rapidly became entangled with the debate over human cloning

Ensuing discussion failed to elaborate on the reasons as to why cloning was developed



Dolly the cloned sheep kills a lamb — and EATS it!

By MIKE FOSTER / Weekly World News

EDINBURGH, Scotland — A frightened scientist says Dolly the cloned sheep has killed a young lamb — and eaten it!

What's more, the world's first cloned mammal has exhibited other strange behavior, such as chasing a young child, biting a keeper and staring menacingly at razzled scientists.

"When you do something to nger her, she looks at you

eyes full of hate," said a researcher involved in the cloning project.

Dolly's eerie antics — including the "cannibalism" episode

two months ago. "A keeper was giving her a bath, which she doesn't seem to enjoy very much," recalled the researcher. "When his back was turned, she bowled him over, then nipped his face, drawing blood.

"Another time I brought my 8-year-old daughter to see Dolly in her pen. She was thrilled and was looking forward to

News

Cloning opens door to 'farmyard freaks'

By SEAN POULTER - More by this author »
Last updated at 08:35am on 11th January 2007

Comments (38)

Moves to clone and genetically modify farm livestock have opened the door to the creation of "Farmyard Freaks", experts have warned.

News that the daughter of a US clone cow has been born on a British farm has moved the issue from science fiction to consumer reality.

A former government adviser has painted a nightmarish picture of "zombie" and fast-growing supersize animals.

Professor Ben Mepham, of Nottingham University, said the impact of bio-engineering, creating GM and cloned animals, is huge.

Factory farming techniques, most commonly used with pigs and chicken, often involve keeping animals confined in cramped conditions.

For pigs, who are highly intelligent, these conditions can lead to stress and aggression.

However, GM scientists are actively investigating ways to remove the stress and aggression gene from animals, effectively turning them into complacent zombies.

The professor said it might become

The cloned cow Dundee Paradise
ENLARGE

Cloning and genetic engineering may be disconcerting to the public….but so is hybrid corn and cross-breeding!

Most of New Jersey's citizens (59%) approve of producing hybrid plants by using traditional cross-fertilization techniques. **However, one-in-five people (20%) believes that it is morally wrong to produce new plants in this way.**

Producing hybrid animals through cross-breeding is viewed even more negatively. Most people (62%) in New Jersey disapprove of producing hybrid animals using this method and half (50%) believe that it is morally wrong

Biotechnology attitudes survey - New Jersey, 1993. Rutgers
http://ageconsearch.umn.edu/bitstream/18170/1/pa94ha01.pdf

Need to defend the ability to use all biotechnologies and production methods…

PRODUCT OF AN ARTIFICIAL SPECIES SELECTIVELY BRED FROM THE NOW-EXTINCT AUROCHS, CROSSBRED STEER CONCEIVED IN A PETRI DISH AFTER MULIPLE OVULATION OF DAM AND EMBRYO TRANSFER, SIRED BY THE OFFSPRING OF A CLONE, GESTATED IN A SURROGATE COW, CASTRATED IN THE ABSENCE OF ANAESTHETIC, IMMUNIZED WITH A RECOMBINANT DNA VACCINE, TREATED FOR PINK EYE WITH LA 200, FINISHED ON GENETICALLY-MODIFIED CORN FOR 90 DAYS, HUMANELY KILLED WITH A CAPTIVE BOLT

CASE STUDY

The following scenario was presented to the UC Davis Chancellor's Ladies' Luncheon in 2008

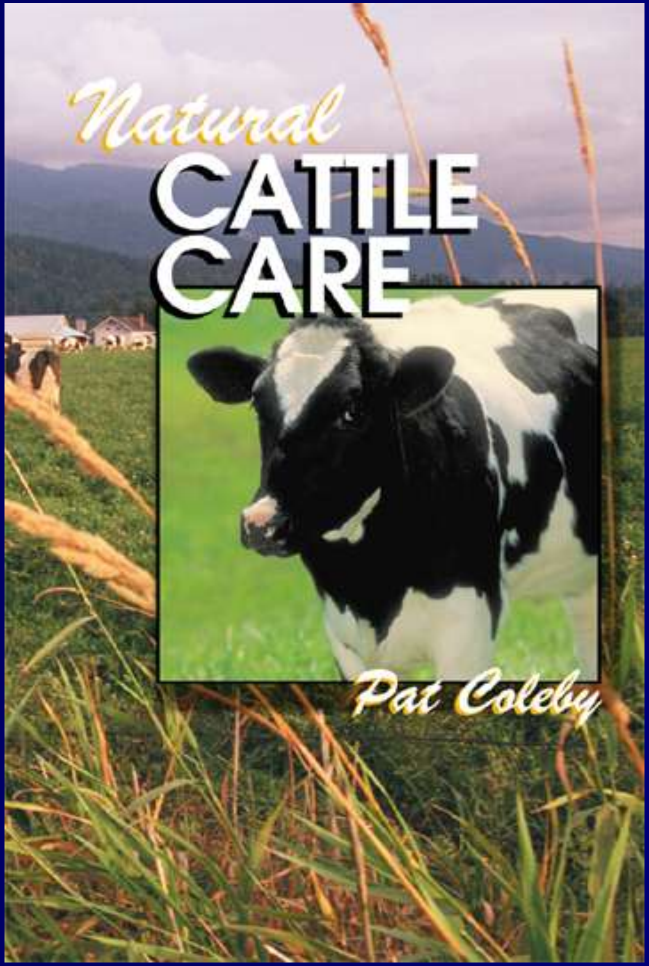
"Which technology would you select to deal with the issue of mastitis in dairy cows?"

CASE STUDY: MASTITIS

inflammation of the mammary gland

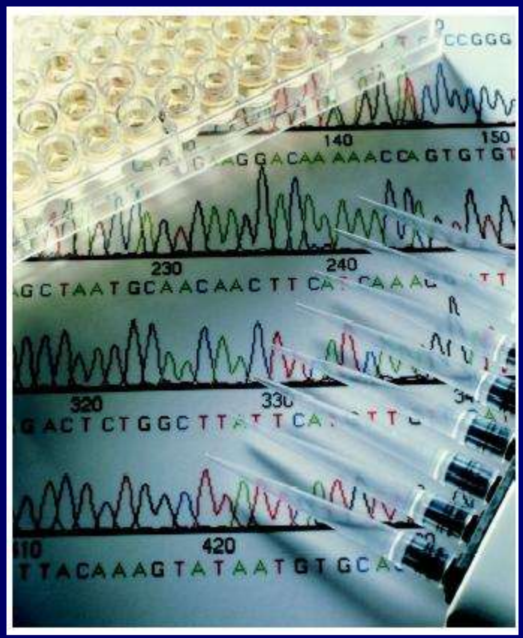
1. Conventional: Antibiotic therapy

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. <u>Genomic Selection</u> (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 bact

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

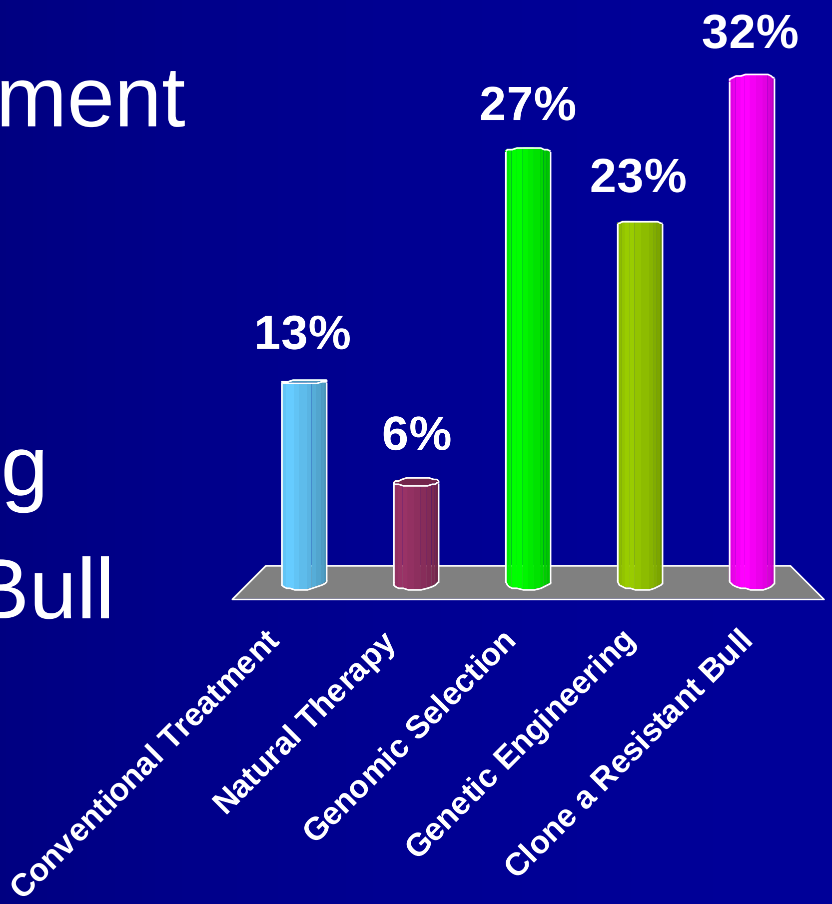
While all milk contains several naturally occurring antimicrobial proteins, such as lysozyme and la

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.

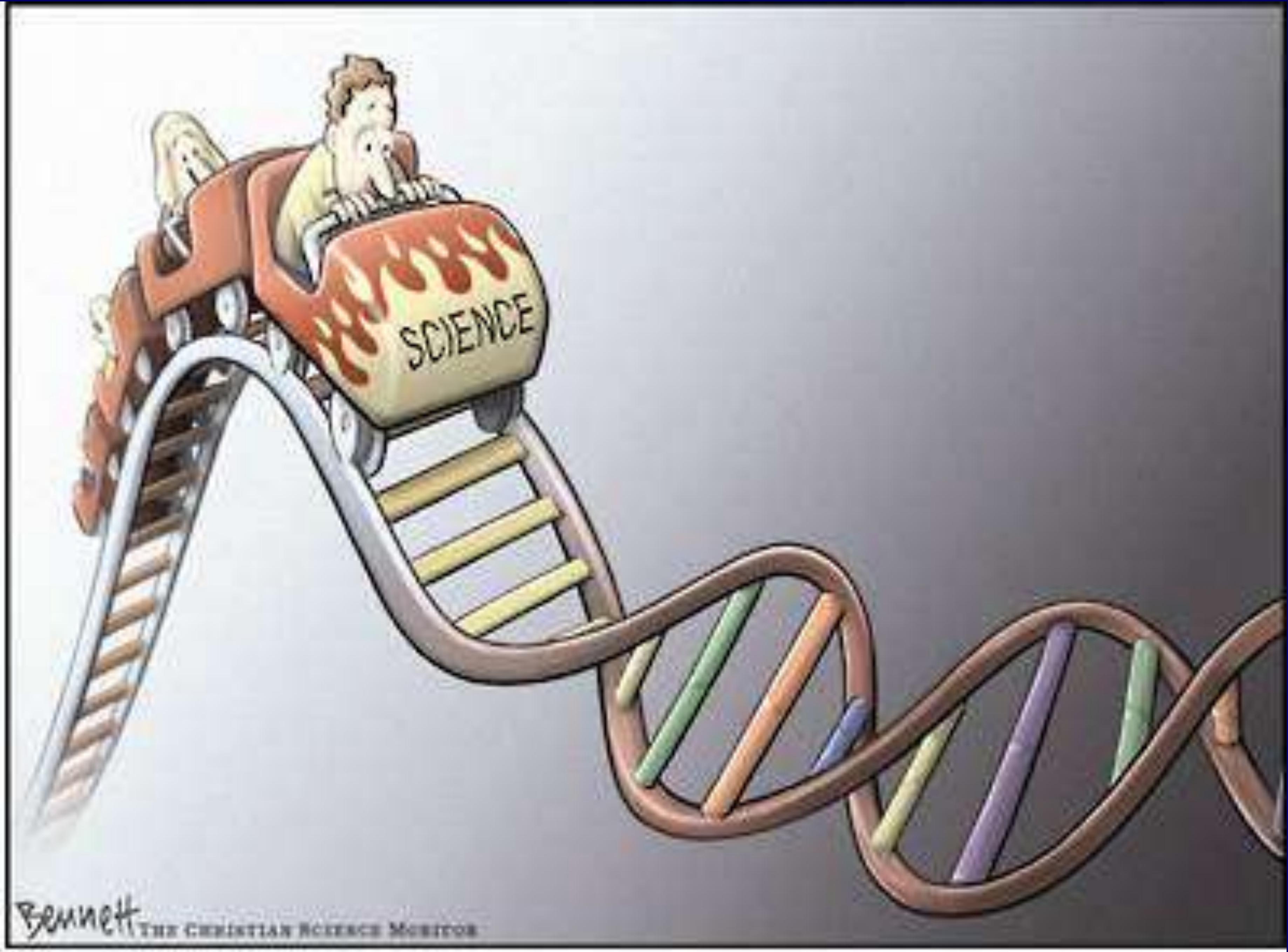
Which Animal Biotechnology would you use?

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



"While animal genetics alone will not solve the world's future food problems, to fail to apply the best available technologies to the solution of contemporary and future food shortages would be morally reprehensible."

Fahrenkrug SC, Blake A, Carlson DF, Doran T, Van Eenennaam A, Faber D, Galli C, Gao Q, Hackett PB, Li N, Maga EA, Muir WM, Murray JD, Shi D, Stotish R, Sullivan E, Taylor JF, Walton M, Wheeler M, Whitelaw B, Glenn BP. 2010. Precision Genetics for Complex Objectives in Animal Agriculture. J. Anim Sci. 88(7):2530-9.


SCIENCE
Bennett THE CHRISTIAN SCIENCE MONITOR