Genomic Selection

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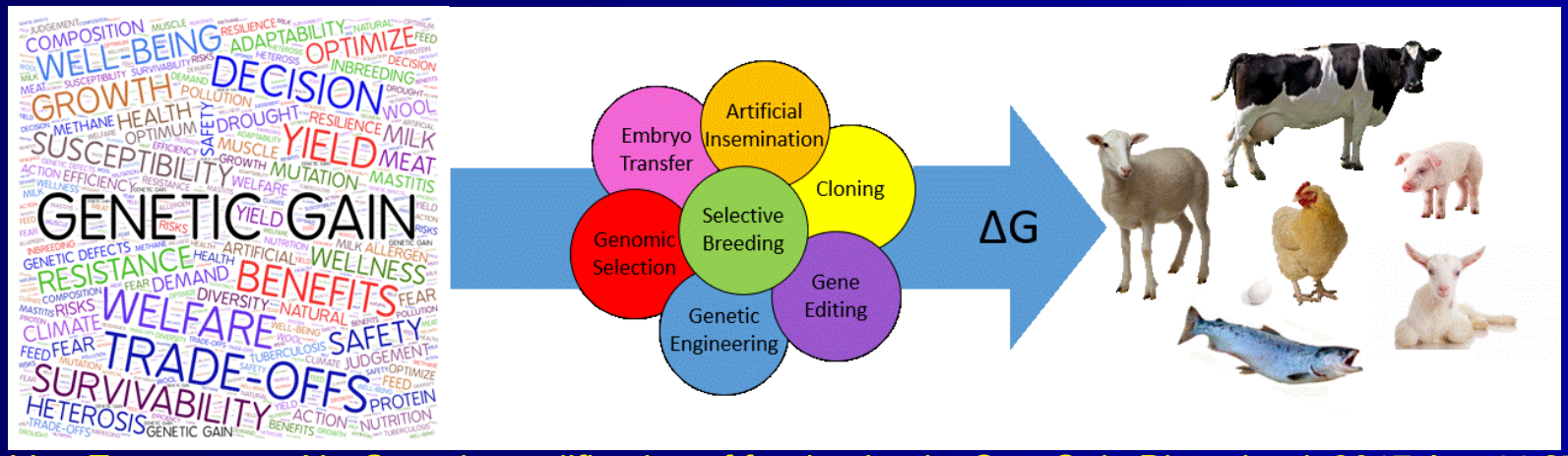


Van Eenennaam AL. Genetic modification of food animals. Curr Opin Biotechnol. 2017 Apr;44:27-34.

Animal breeders have used selection on phenotypes to great effect!



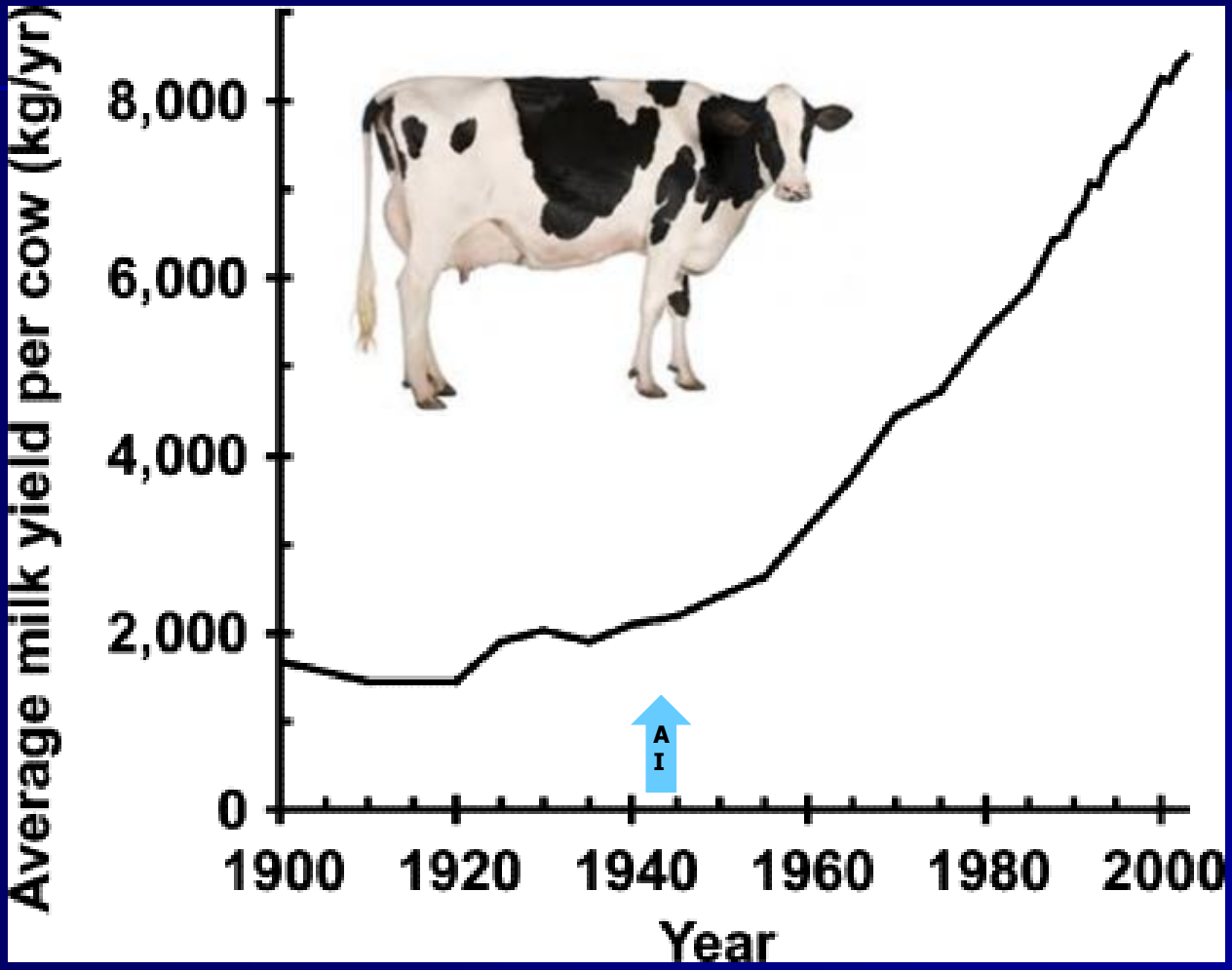



However breeding based on objective performance recording has been spectacularly successful…..

Havenstein, G., Ferket, P. and Qureshi, M. (2003). Growth, livability, and feed conversion of 1957 versus 2001 broilers when fed representative 1957 and 2001 broiler diets. *Poultry Science* 82, 1500-1508.

1944: 25.6 million animals; total annual milk production of 53.1 billion kg.
1997: 9.2 million animals; total annual milk production of 84.2 billion kg.

About half of this 369% increase in production efficiency is attributable to genetic improvement enabled by AI

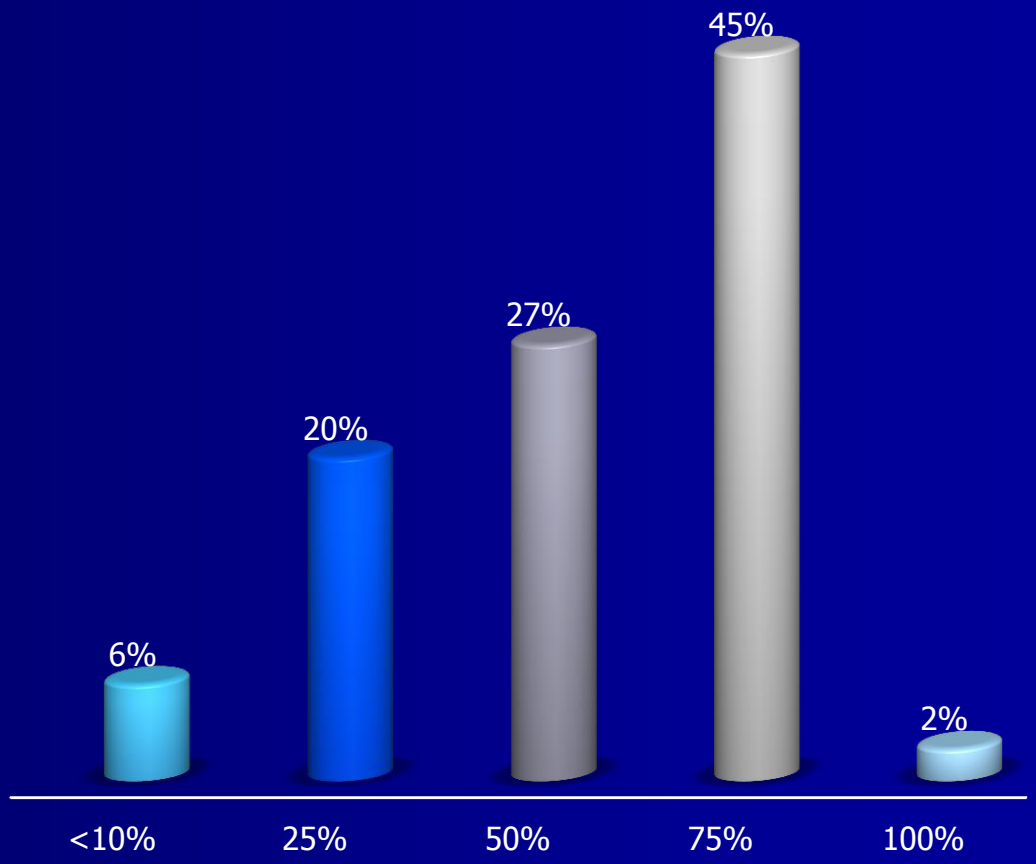


VandeHaar, M.J. and St-Pierre, N. (2006). Major Advances in Nutrition: Relevance to the Sustainability of the Dairy Industry. *Journal of Dairy Science* 89, 1280-1291.

What weighting is given to milk production in the current US dairy cattle economic selection index?

What weighting is given to milk production in the selection of dairy cattle?

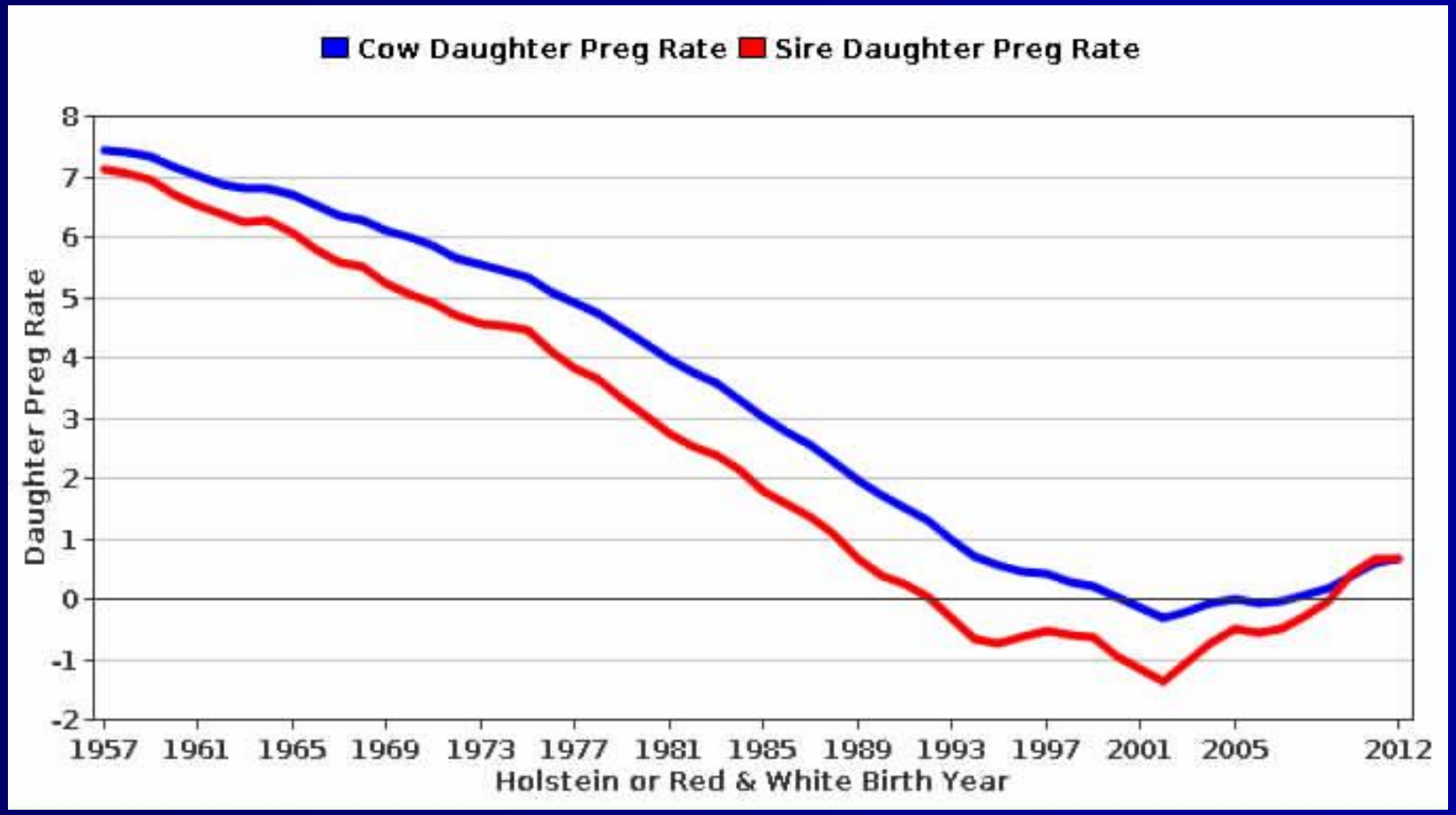
A. <10%
B. 25%
C. 50%
D. 75%
E. 100%



History of the main changes in USDA selection indexes for dairy cattle and % relative emphasis on traits included in the index

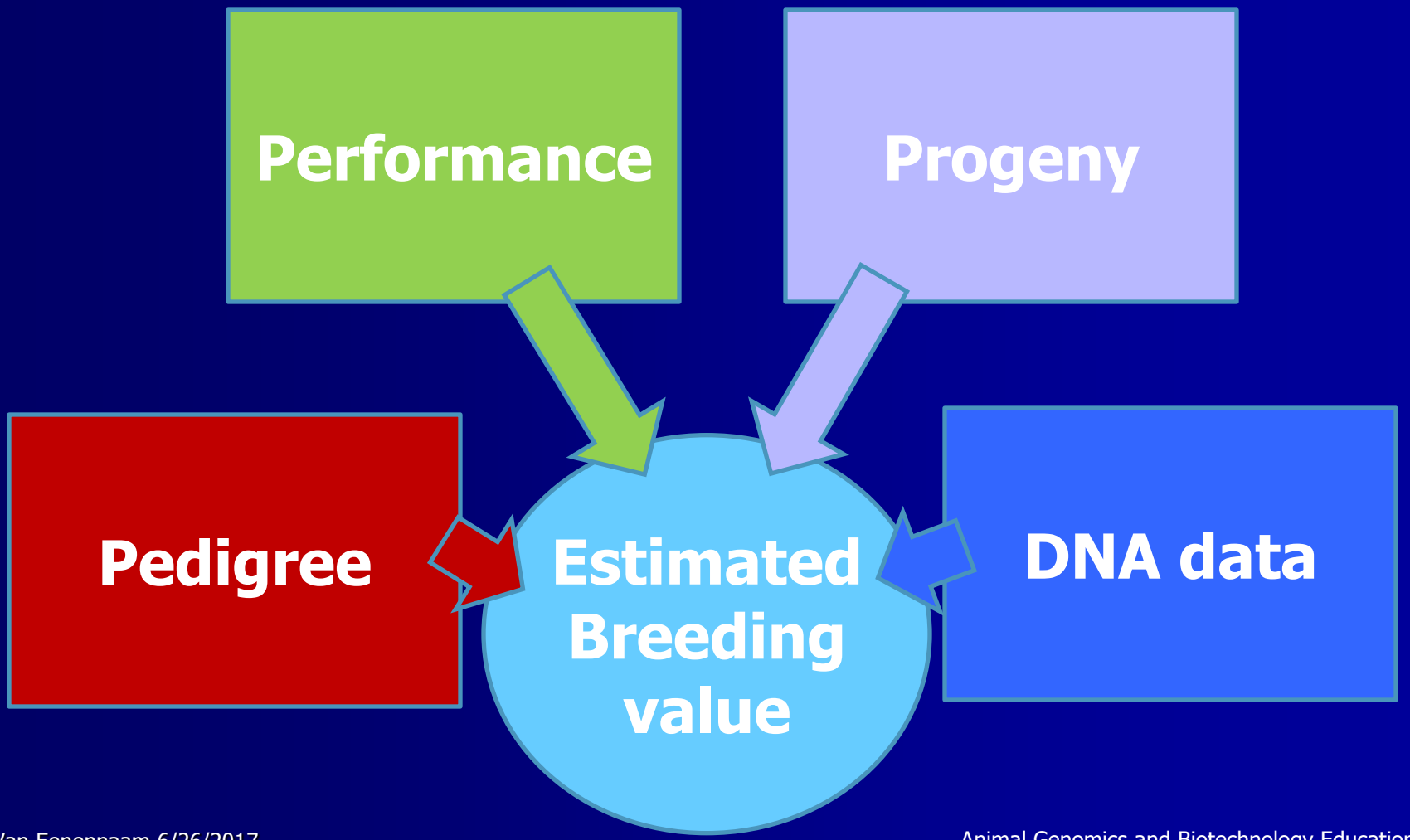
Traits included	USDA genetic-economic index (and year introduced)								
	PD$ (1971)	MFP$ (1976)	CY$ (1984)	NM$ (1994)	NM$ (2000)	NM$ (2003)	NM$ (2006)	NM$ (2010)	NM$ (2014)
Milk	52	27	−2	6	5	0	0	0	**−1**
Fat	48	46	45	25	21	22	23	19	**22**
Protein		27	53	43	36	33	23	16	**20**
Productive life				20	14	11	17	22	**19**
Somatic cell score				−6	−9	−9	−9	−10	**−7**
Udder composite					7	7	6	7	**8**
Feet/legs composite					4	4	3	4	**3**
Body size composite					−4	−3	−4	−6	**−5**
Daughter pregnancy rate						7	9	11	**7**
Cow conception rate									**2**
Heifer conception rate									**1**
Calving ability							6	5	**5**

Genetic trend in daughter pregnancy rate for U.S. Holstein or Red & White dairy cattle since the inclusion of this fertility trait in the dairy selection index in 2003.



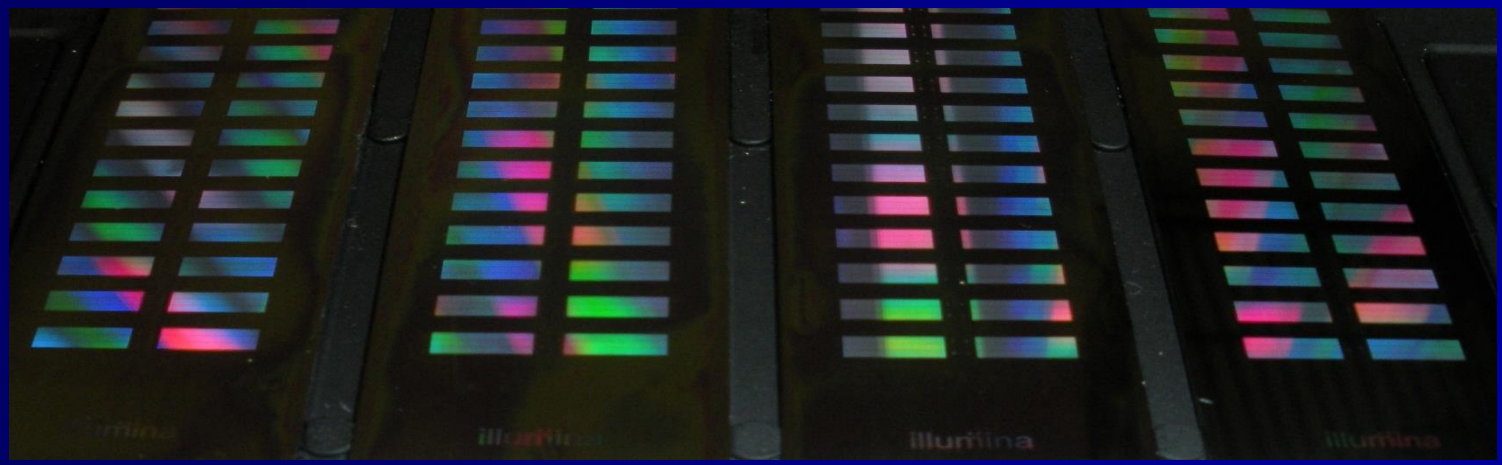
Graph available at: https://www.cdcb.us/eval/summary/trend.cfm?R_Menu=HO.d

Information sources for estimated breeding value (EBV) genetic merit – DNA just one source of data



High-throughput genotyping technology enabled the development of high density "SNP chips"

The sequencing of the bovine genome allowed for the development of a 50,000 SNP chip, then the 800,000 SNP chip; and now whole genome sequence (3 billion)!



We can use these SNP CHIPS for "genomic" selection?

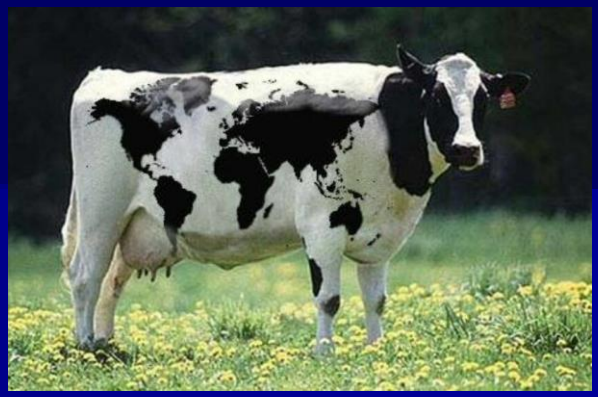
TRAINING POPULATION

1,000s animals
- 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 develop prediction equations to predict the merit of new animals (e.g. young bulls)

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

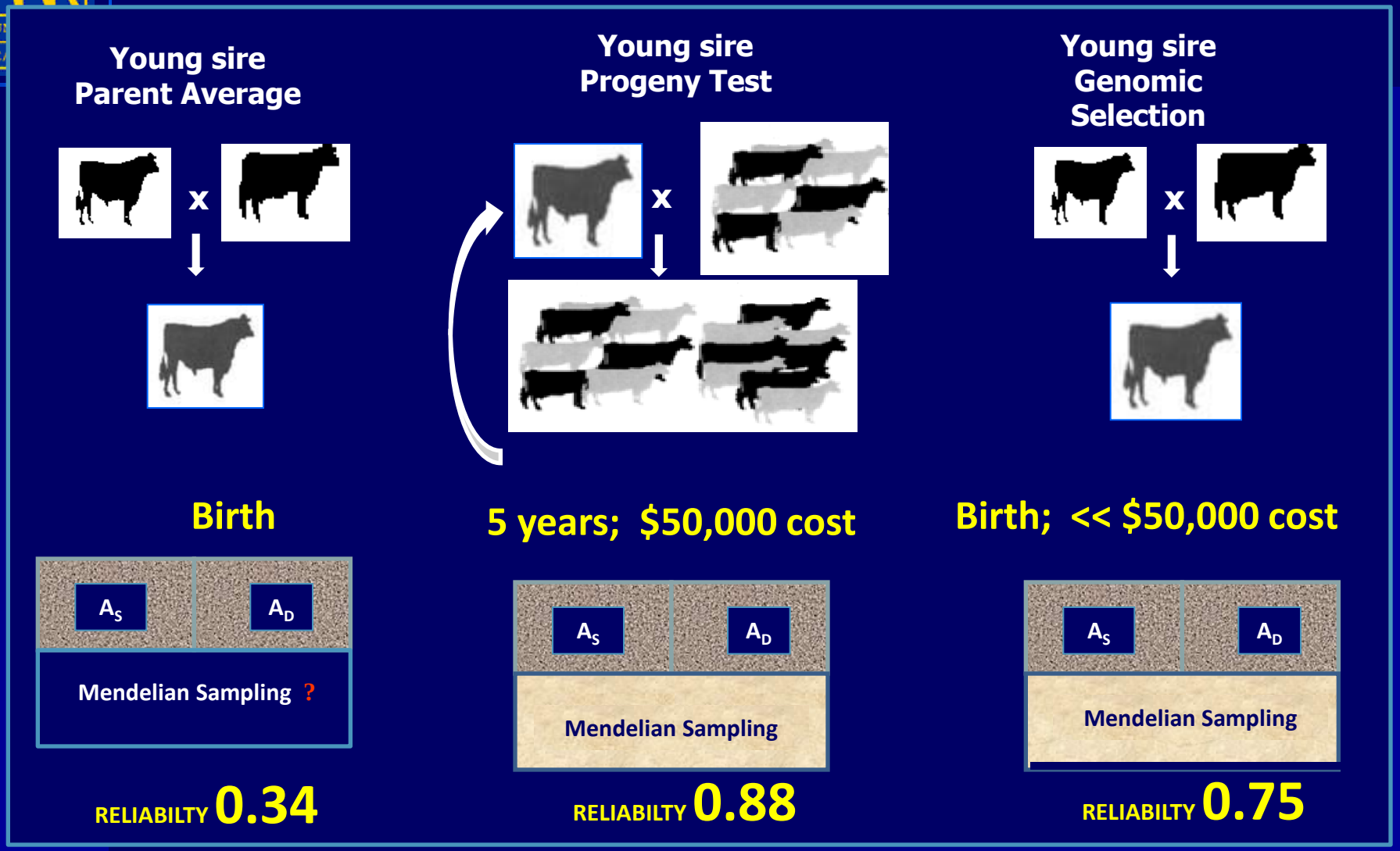
Records in US dairy database

Pedigree records	71,974,045
Animal genotypes	1,035,590
Lactation records (*since 1960*)	132,629,200
Daily yield records (*since 1990*)	641,864,015
Reproduction event records	179,559,035
Calving difficulty scores	29,528,607
Stillbirth scores	19,567,198

Data from George Wiggins, USDA ARS (7/2015)

Breeding value prediction in Dairy Sires

Graphic kindly provided by Gonzalo Rincon



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

$= (2*0.93 + 0)/ (6+2)$ = 0.23 s.d./year (progeny test)

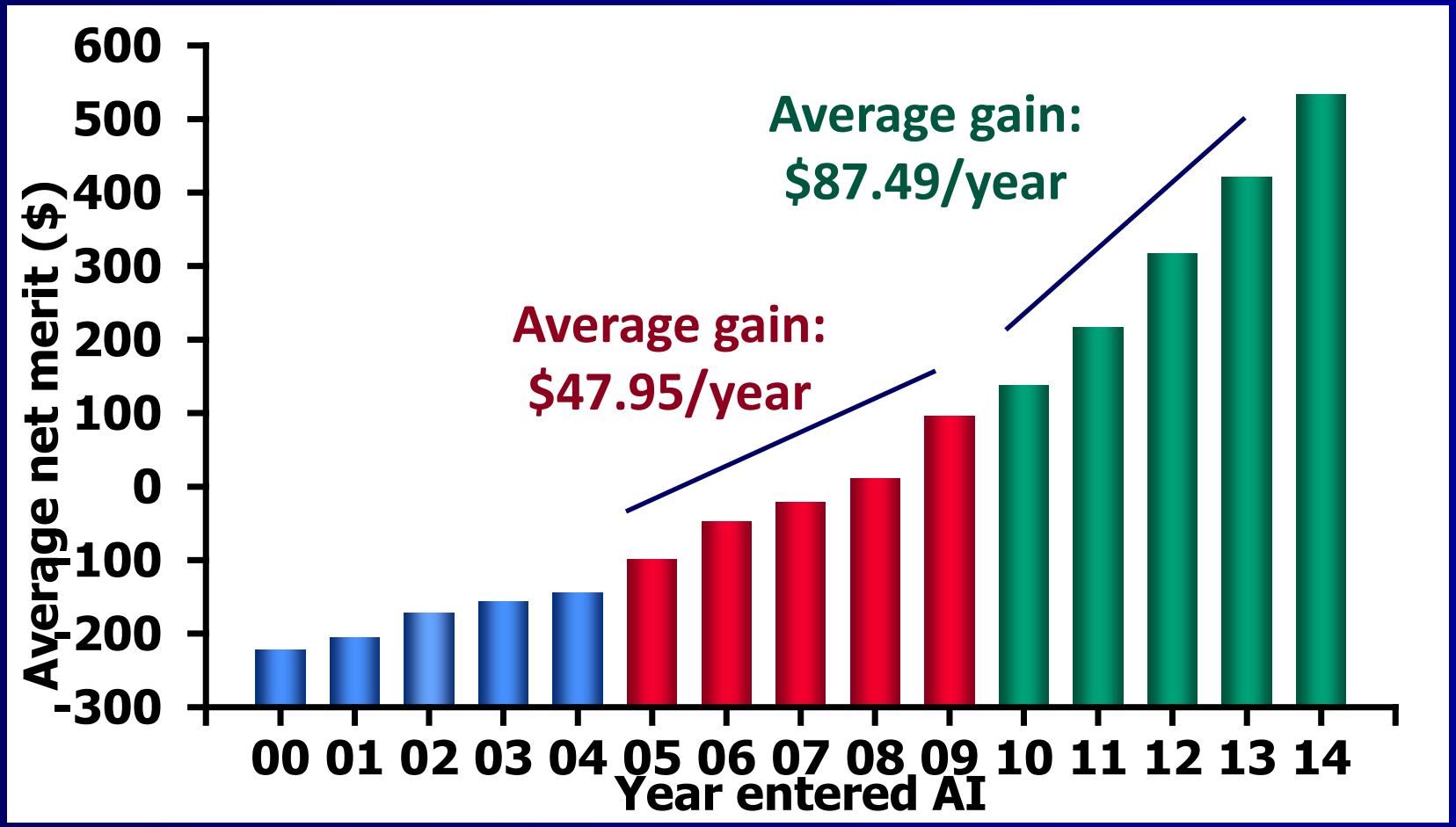
$= (2*0.87 + 0.8*0.87)/ (2+2)$ = 0.61 (genomic selection)

i = intensity of selection

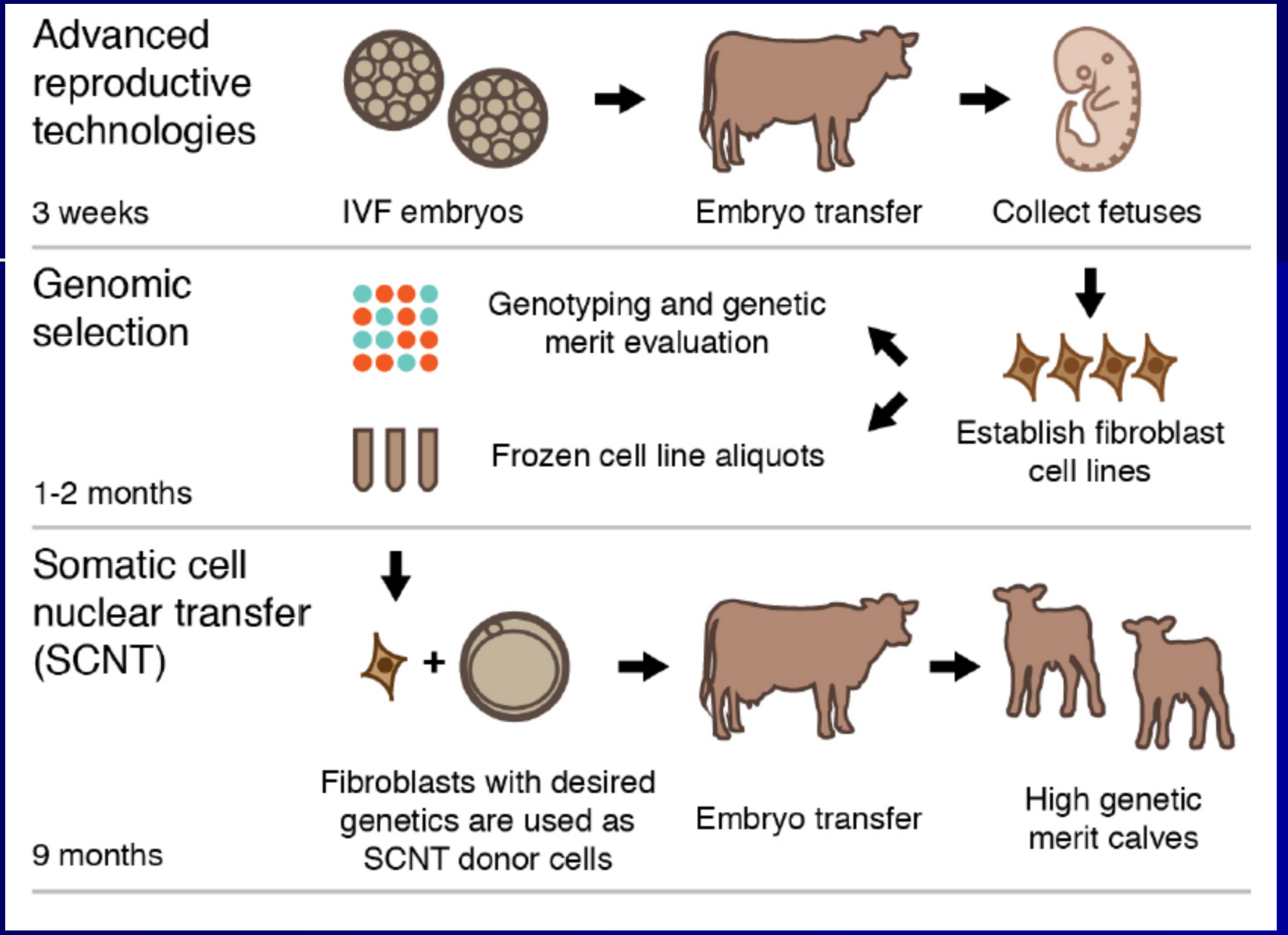
r = accuracy of selection

L = generation interval

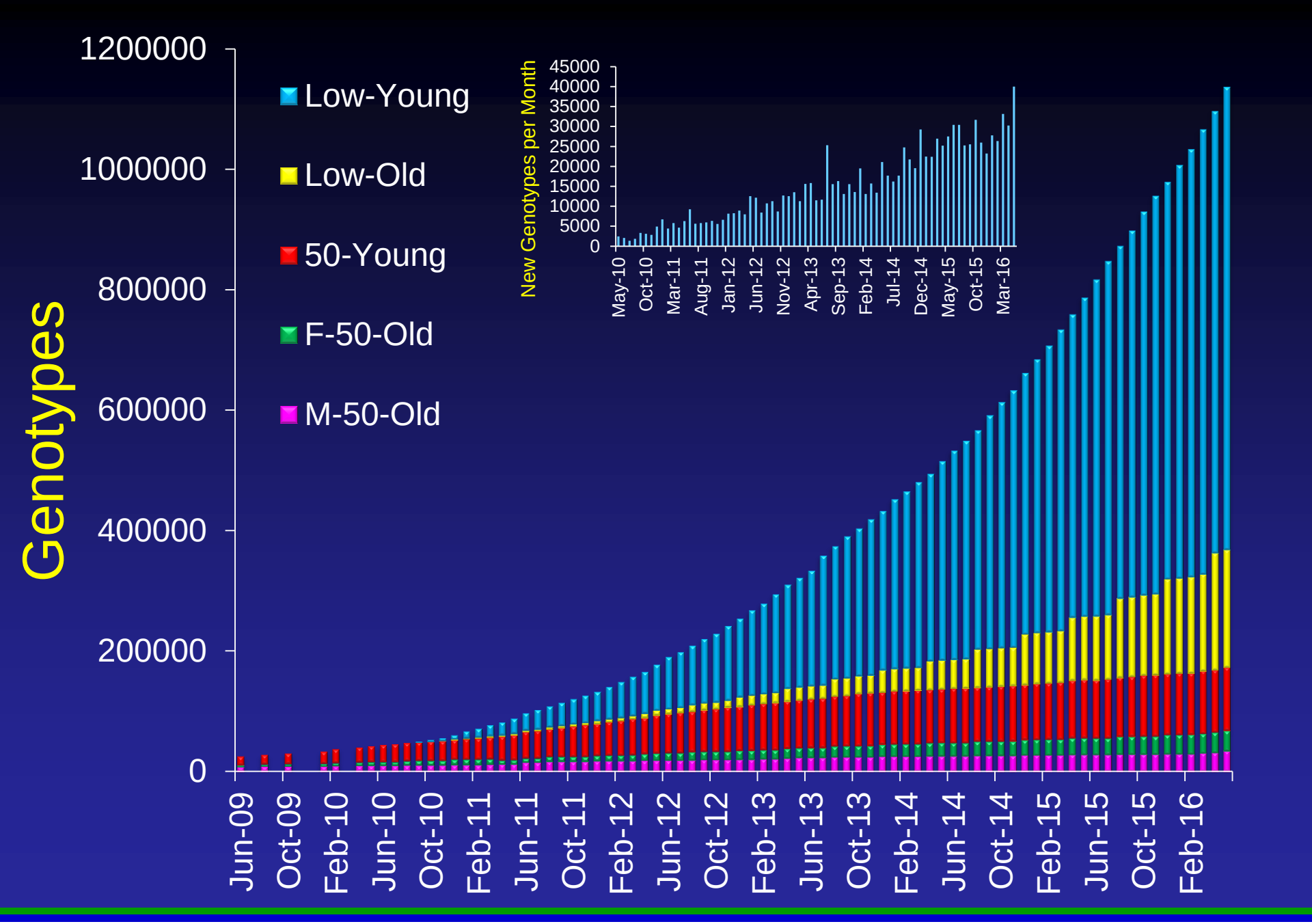
Rate of genetic gain in marketed Holstein bulls has doubled since 2009 genomic selection introduction



Data from George Wiggins, USDA ARS (7/2015)



Kasinathan, P. *et al.* 2015. **Acceleration of genetic gain in cattle by reduction of generation interval.** Sci. Rep. 5, 8674; DOI:10.1038/srep08674


Genotypes
1200000
1000000
800000
600000
400000
200000
0
Low-Young
Low-Old
50-Young
F-50-Old
M-50-Old
New Genotypes per Month
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
May-10
Oct-10
Mar-11
Aug-11
Jan-12
Jun-12
Nov-12
Apr-13
Sep-13
Feb-14
Jul-14
Dec-14
May-15
Oct-15
Mar-16
Jun-09
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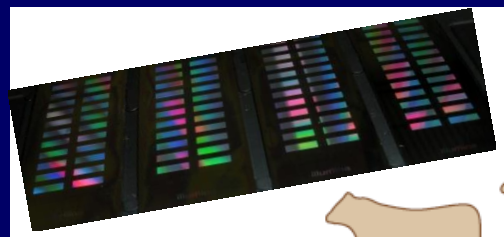


Large training population
- Phenotyped
- Genotyped

Phenotypes

Genotypic and phenotypic information from selected animals used to recalibrate marker effects to maintain prediction equation accuracy

Predict genetic merit of selection candidate within breed based on genotype

Factors that improve accuracy of GS:
- Large number of animals in training population
- Number of SNP markers being genotyped
- Small effective population size
- High heritability of the trait to be improved
- Small number of large-effect QTL influencing trait
- High level of genetic relationship between training and selection candidates

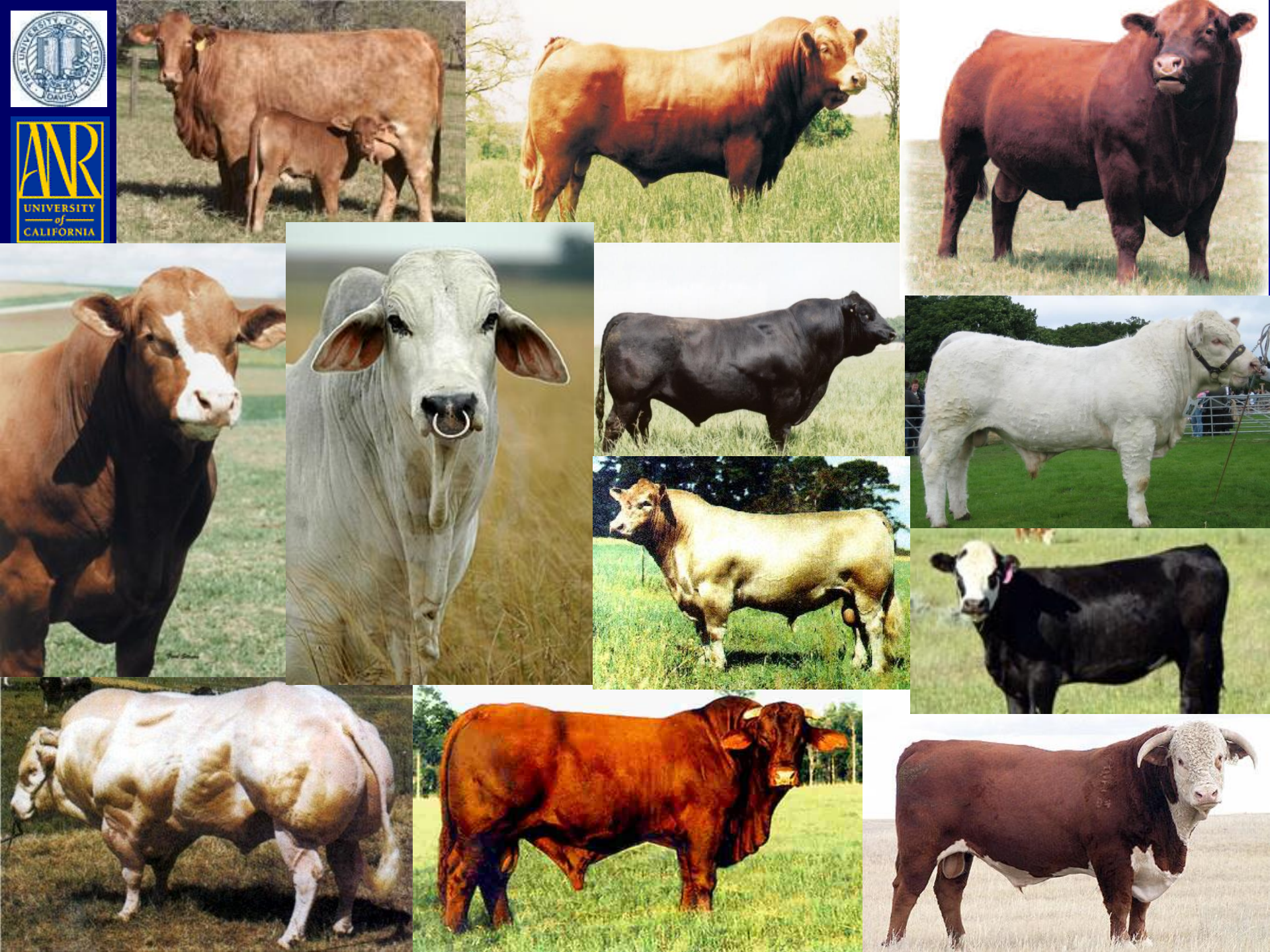
Estimate marker effects for phenotyped traits

Predict genetic merit of selection candidate within breed based on genotype

Not predictive in other breeds/strains/lines

Selection candidate population
Genotypes used to predict genetic merit

Van Eenennaam *et al.* 2014. Annu. Rev. Anim. Biosci. 2: 105-139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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

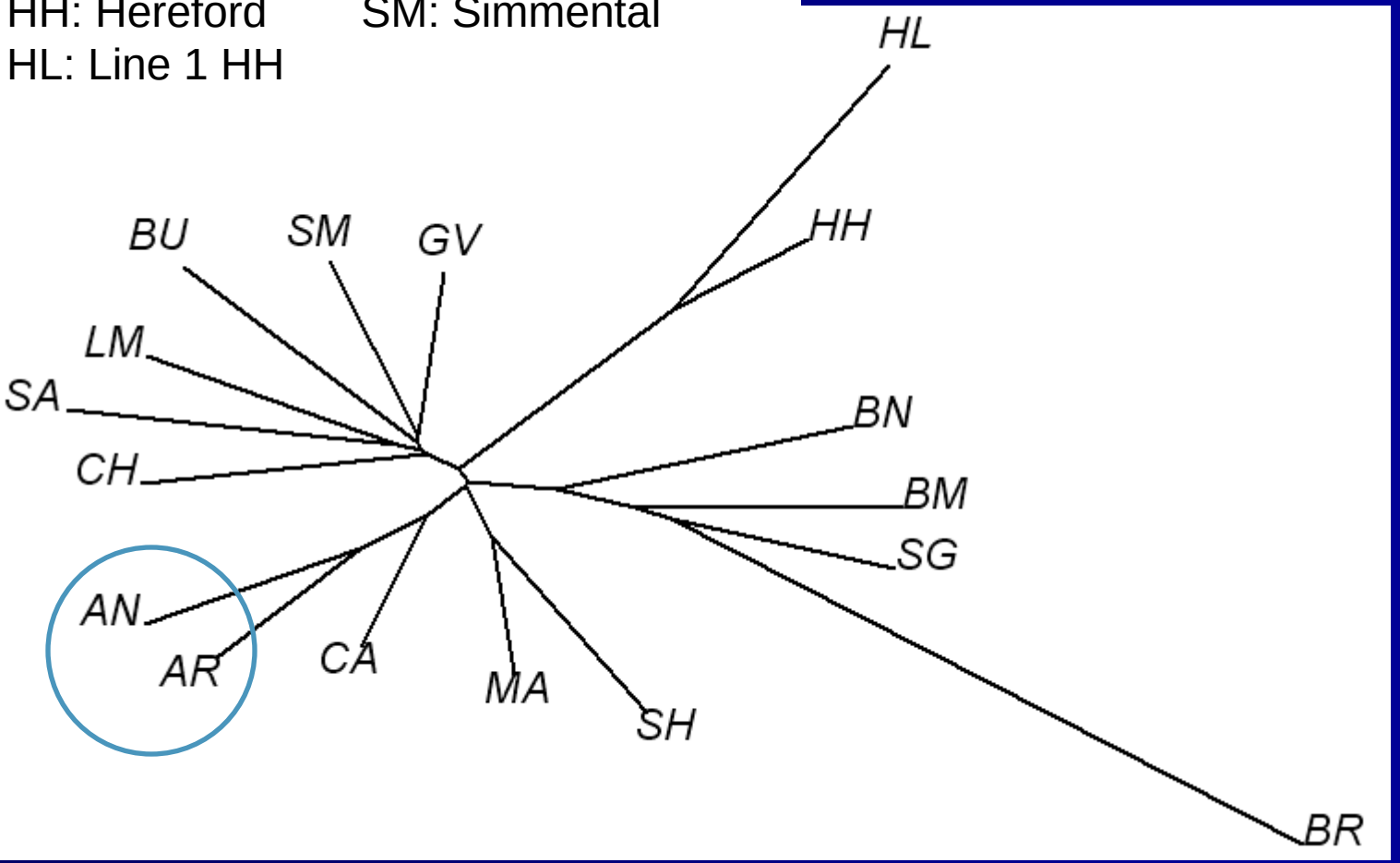
A perfect storm is a confluence of events that drastically aggravates a situation

AN: Angus
BM: Beefmaster
BN: Brangus
BR: Brahman
BU: Braunvieh
CA: Chiangus
CH: Charolais
HH: Hereford
HL: Line 1 HH
GV: Gelbvieh
LM: Limousin
MA: Maine Anjou
RA: Red Angus
SA: Salers
SG: Santa Gertrudis
SH: Shorthorn
SM: Simmental

Approximate genetic distance between breeds using data from the 2,000 Bull Project.

Larry Keuhn, USDA MARC

http://www.nbcec.org/topics/BeefBreeds.pdf



Genomics in US National Beef Cattle Genetic Evaluation

- Currently several breeds are using genomic information in their national cattle evaluation programs (Fall 2016)
  - Angus (264,656) - Hereford (~23,000)
  - Red Angus (22,791) - Gelbvieh (10,162)
  - Limousin (3,340) - Charolais (2,454)
  - Simmental (32,629) - Santa Gertrudis (3,160)
  - Beefmaster - Brangus (3,909)
- Other breeds are trying to incorporate genomic information
- Virtually only National Cattle Evaluation traits – only traits with enough data to train prediction equation

Species

↑ Accuracy
↑ Intensity
↑ Genetic Variation
↓ Generation interval

Tools/Methods Available

Selective Breeding
Genomic Selection
Embryo Transfer
Artificial Insemination
Sterile Insect Technique
Cloning
Genetic Engineering
Genome Editing

Research

Millions of genetically engineered Mice/Laboratory Rodents/Zebrafish

Biomedical Products

Pigs – Xenotransplantation; Blastocyst complementation of organs

Pharma products

Rabbit - Ruconest
Goat – ATryn, spider silk;
Chickens – Kanuma
Cows – polyclonal antibodies

Pets

GloFish
Micropigs

Pest Control

TseTse fly – sleeping sickness
Mosquitoes – zika/malaria resistance
Moths – agricultural pest control

Agriculture/ Food products

AquAdvantage Salmon - fast growth
Disease resistance
Improved product quality
Decrease environmental footprint
Single gender offspring

Thanks for inviting me!

UCDAVIS
ANIMAL SCIENCE

My laboratory receives public funding support from the National Institute of Food and Agriculture and the Biotechnology Risk Assessment Grant (BRAG) program, U.S. Department of Agriculture, under award numbers 2011-68004-30367, 2013-68004-20364, 2015-67015-23316 and 2015-33522-24106.

USDA United States Department of Agriculture National Institute of Food and Agriculture