LOCAL INDUSTRY DAY

Genomic selection in practice:

Application and uses in the U.S. dairy industry

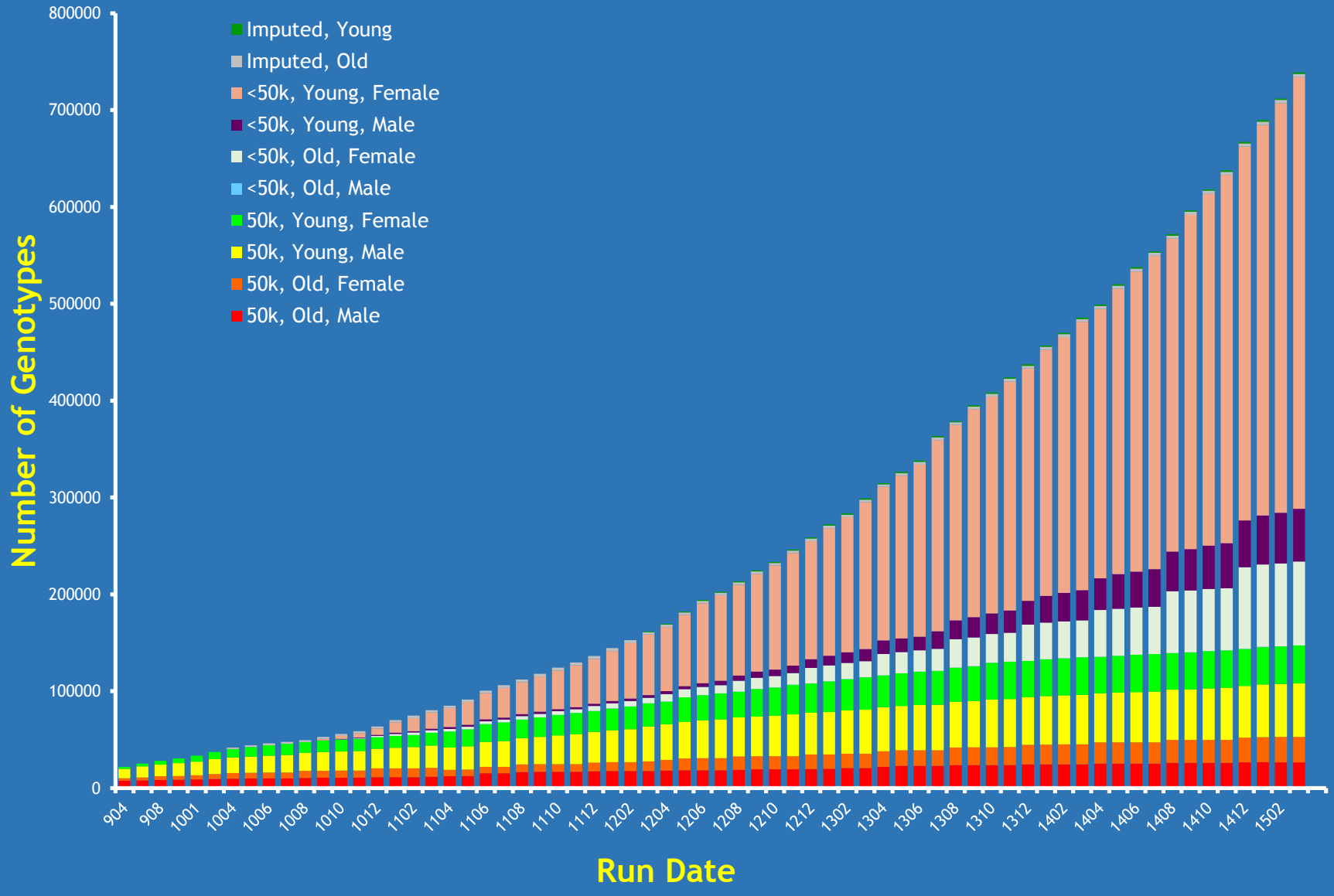
Dr. Tom Lawlor, Holstein USA

U.S. Registered Holsteins
FOR MAXIMUM PROFIT

Genomic information

Has revolutionized the dairy cattle breeding industry.

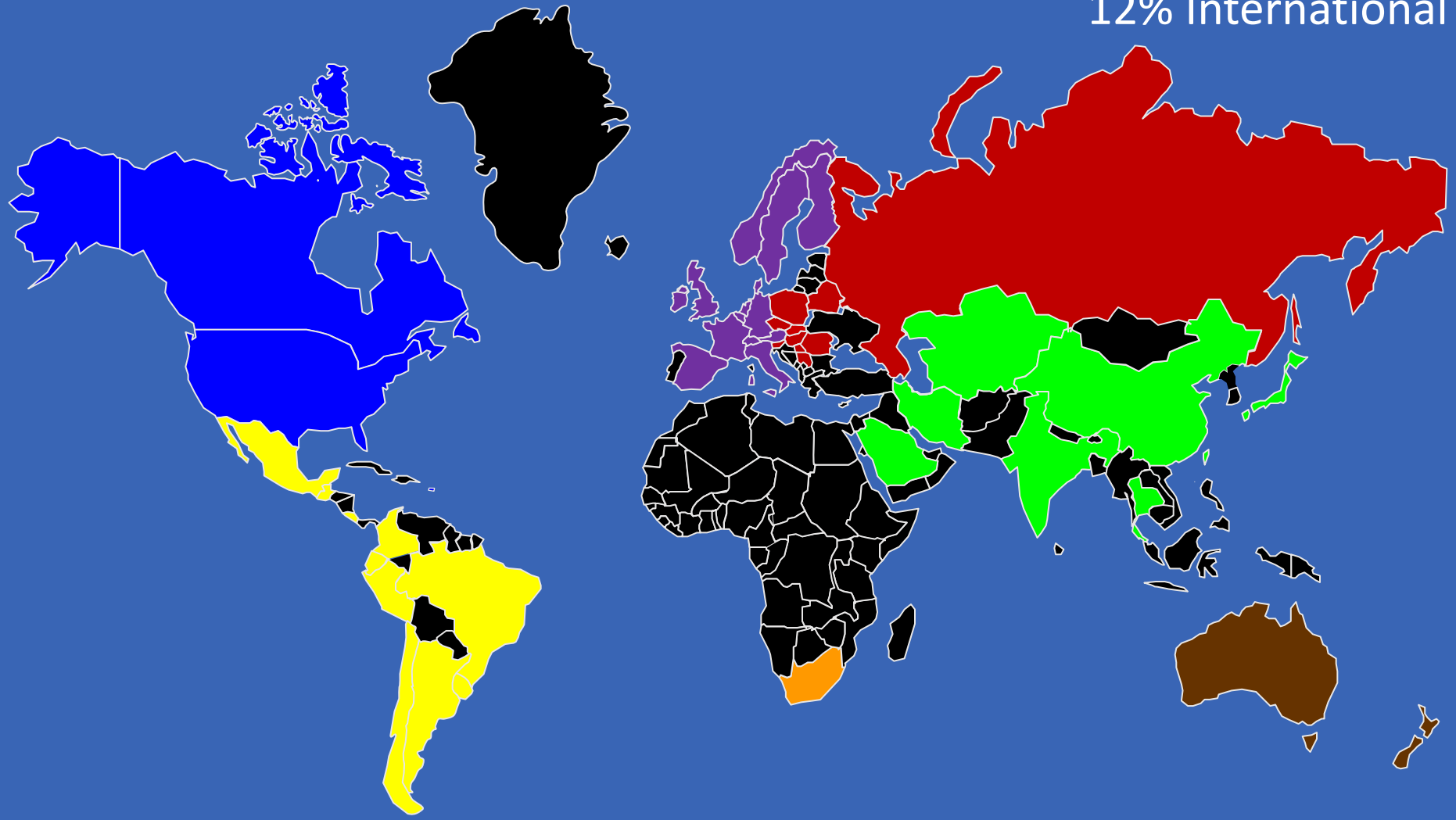
Genomic testing continues to grow in popularity



Genotype Contributors

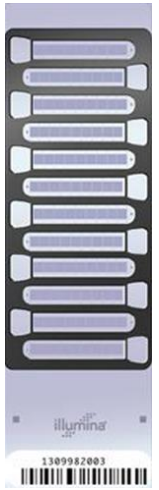
by continent

Over 1 million animals genotyped.
77% from USA,
11% from Canada,
12% International



How we're using genomics within the Holstein breed.

- Determine the **genetic merit** of elite animals at a young age.
- **Herd Management**, cull low end replacement animals earlier, breed lower genetics to beef bulls.
- Verify or discover **Parentage.**
- Identify **Breed composition** of crossbreds. ½ HO, ¼ HO, etc.
- Track **haplotypes** or **single genes**.
- Manage the rate of **Inbreeding.**
- Having more animals genotyped allows us to more easily **investigate** other genetic issues.

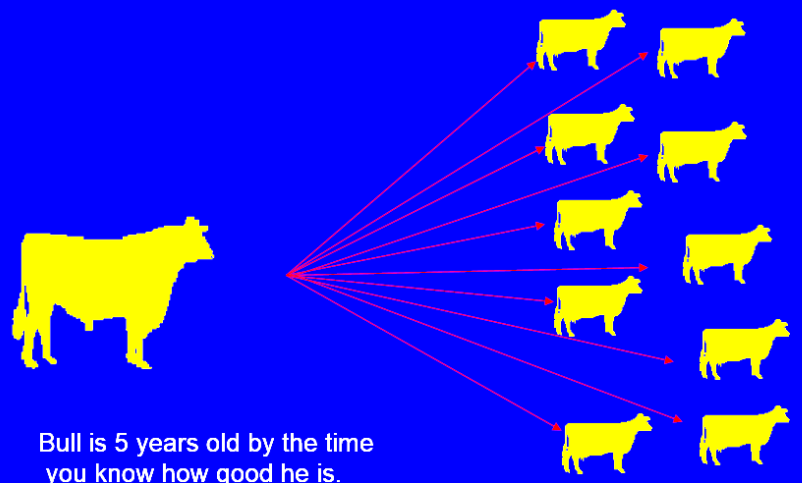


Determine Genetic Merit

Progeny Testing

Distribute semen across the country.

Goal: Get 120 daughters in 80 herds



Bull is 5 years old by the time you know how good he is.

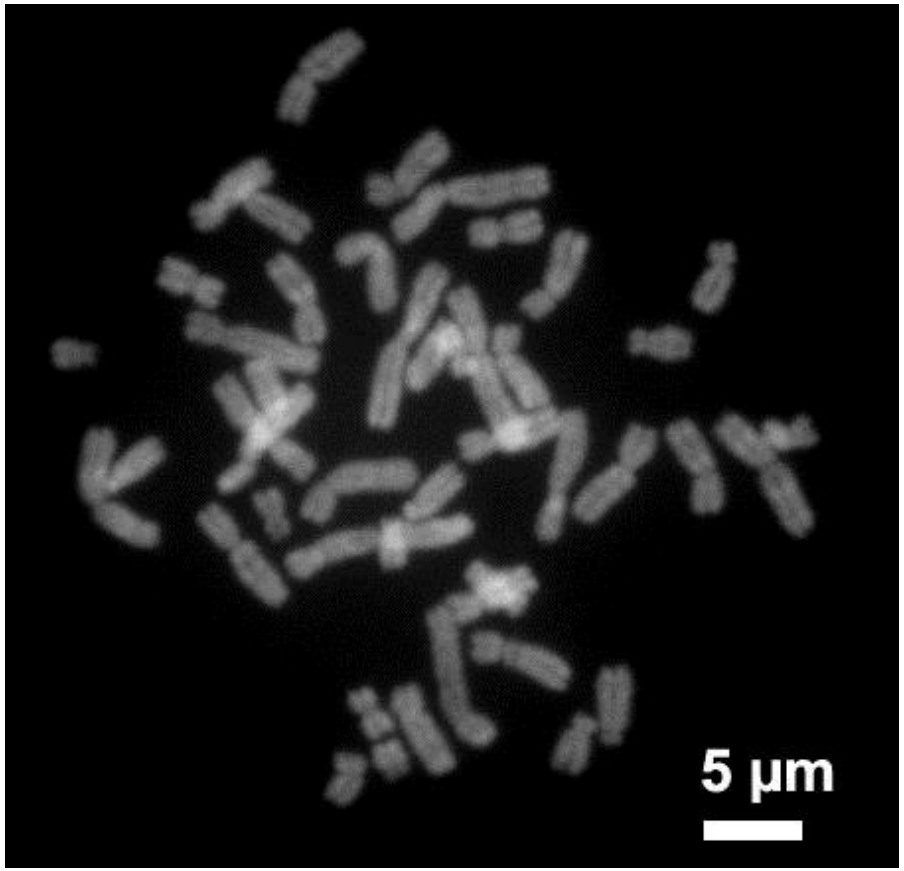
Before having Genomic Predictions

We would predict a the bull's <u>average</u> Transmitting Ability for a trait like Lifetime Net Merit.

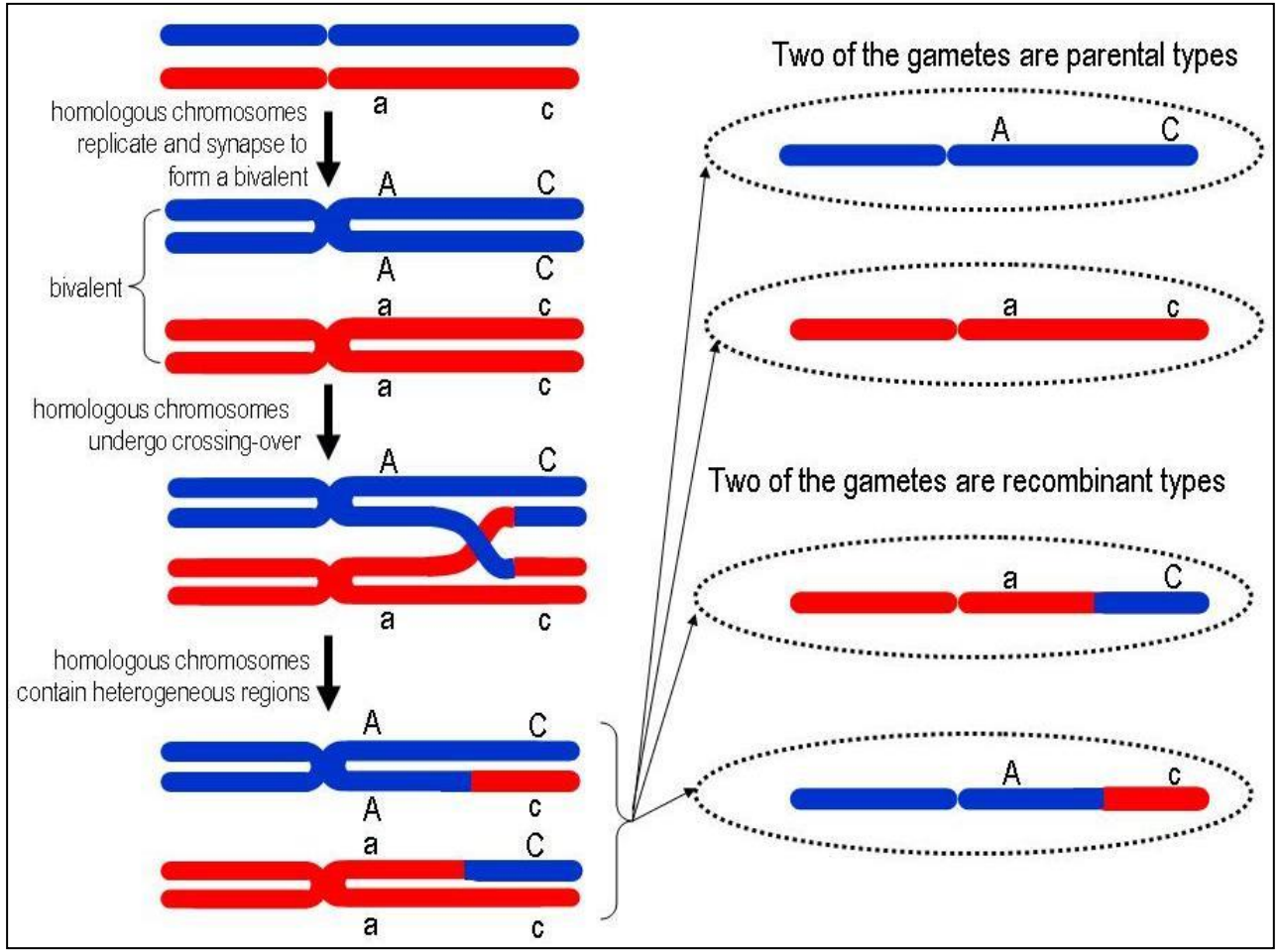
PTA NM$ is **$660**

<u>On average</u> his offspring should produce **$660 more profit than a breed average cow**

DNA isn't transmitted as ONE long piece it's transmitted in sections called chromosomes



Chromosomes frequently break and recombine.

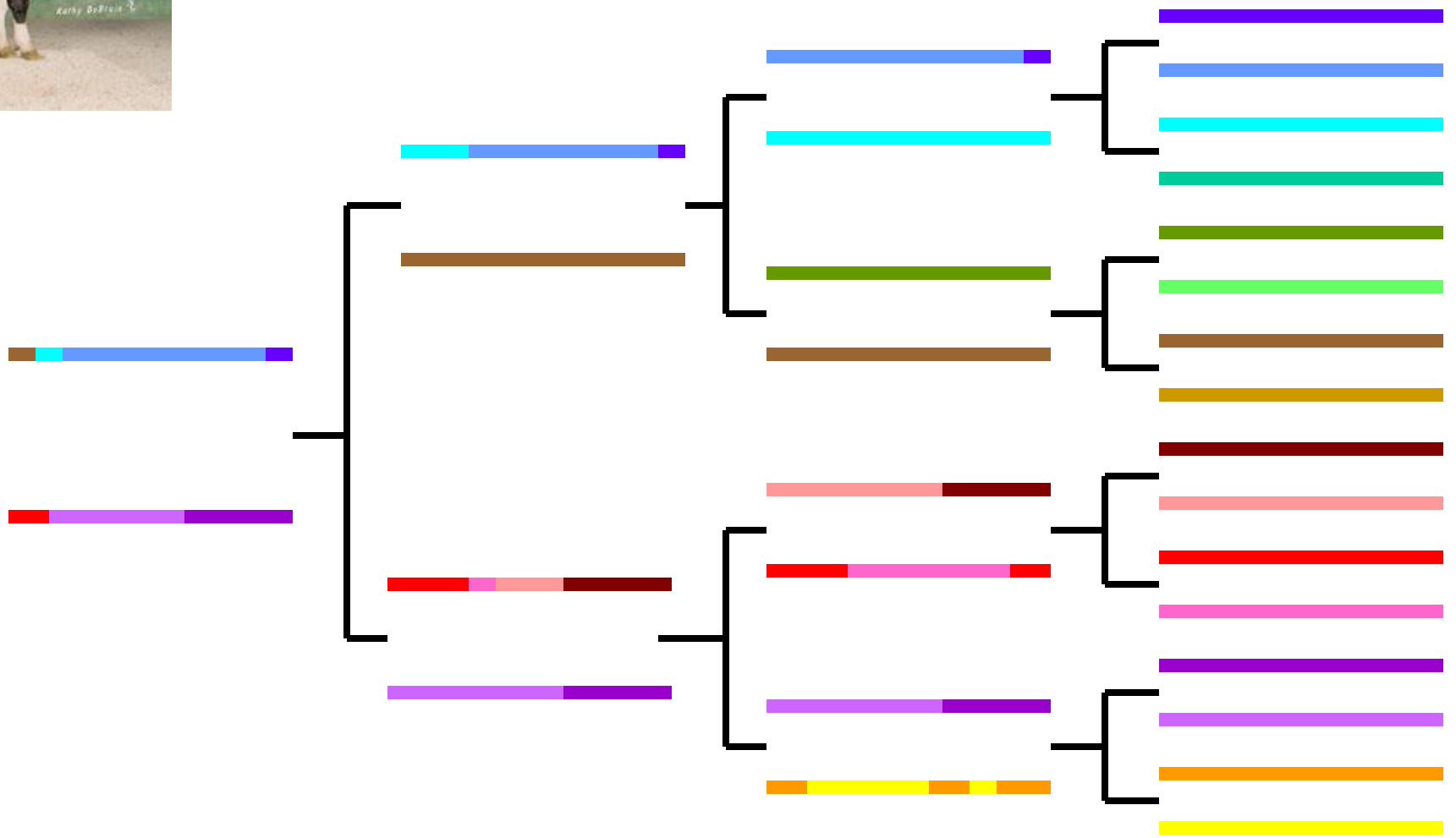


With genomic testing, we're now able to track the inheritance of chromosome segments with the use of genetic markers.

The genetic Markers (SNPs)

GATTCACGCTTACTGTTTCACTGGA

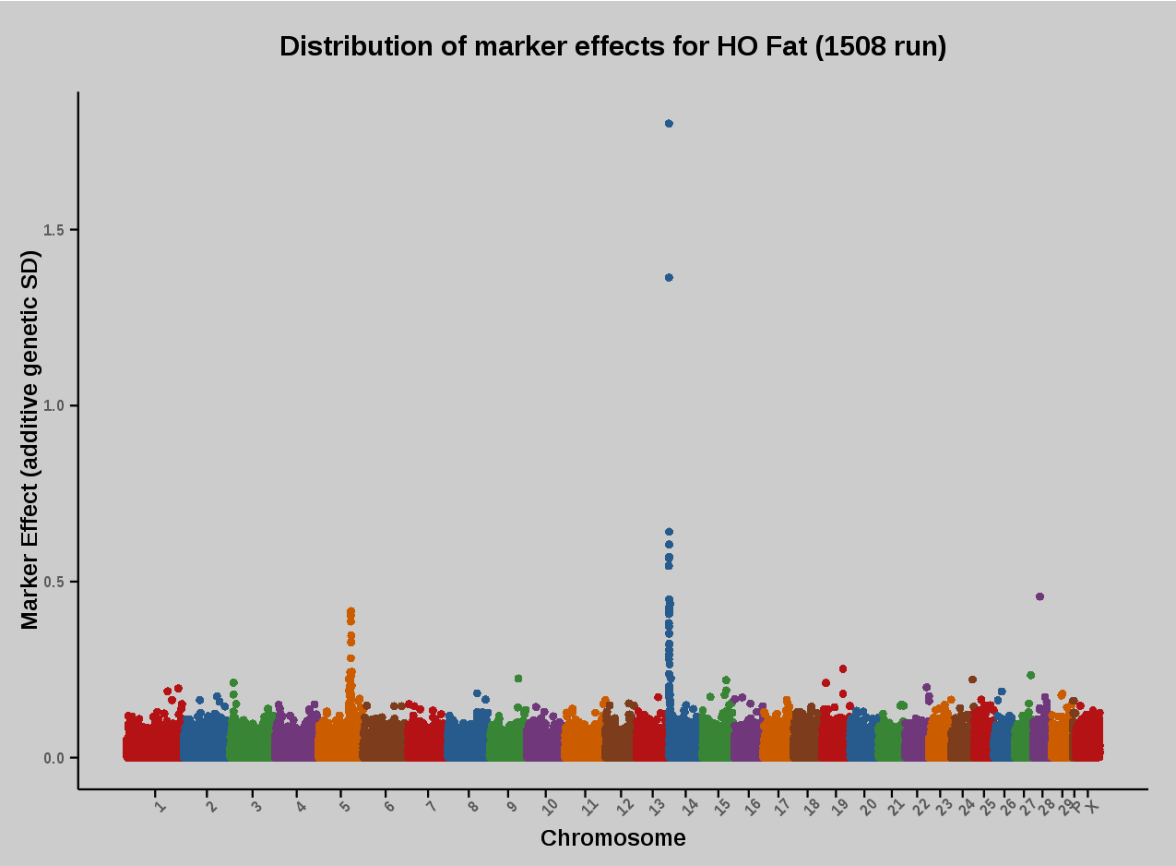
Track haplotypes (sections of DNA) over time



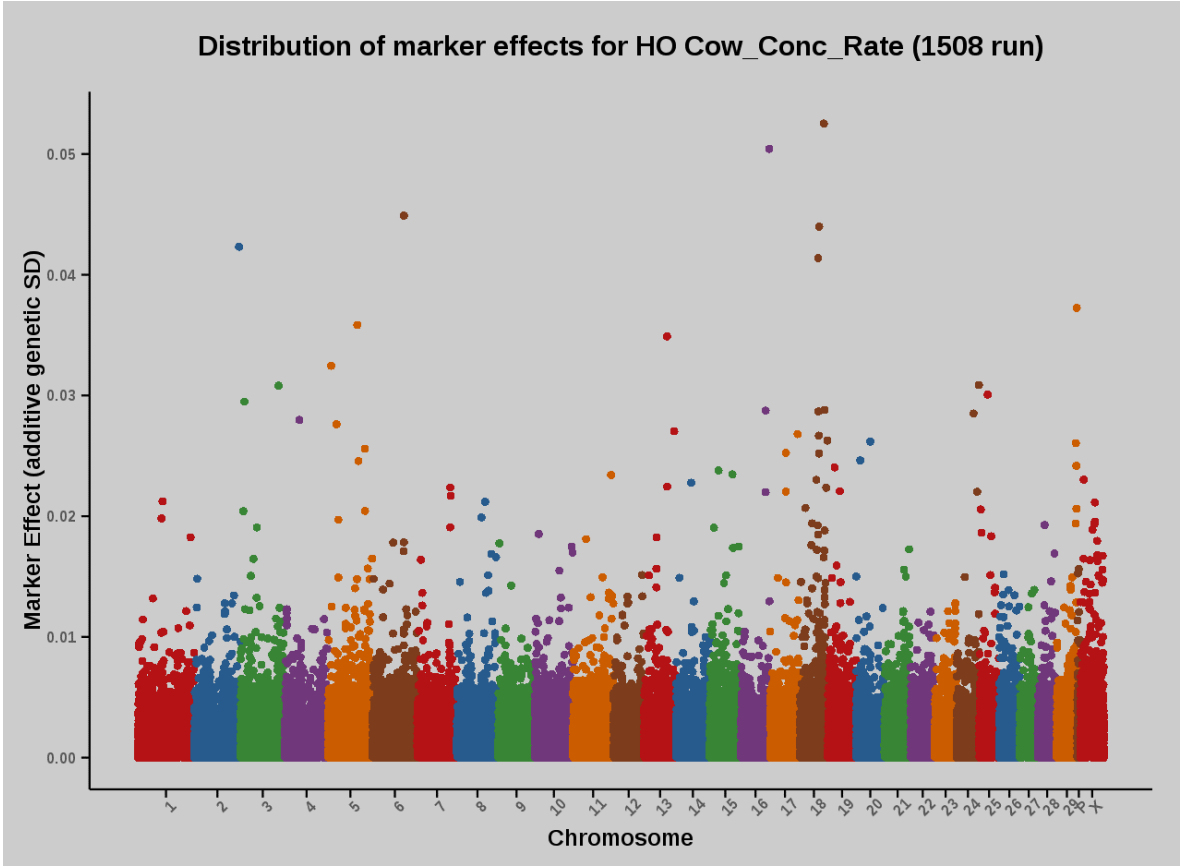
Chromosome 15

We can estimate the value of each section of an animal's genome for a variety of traits

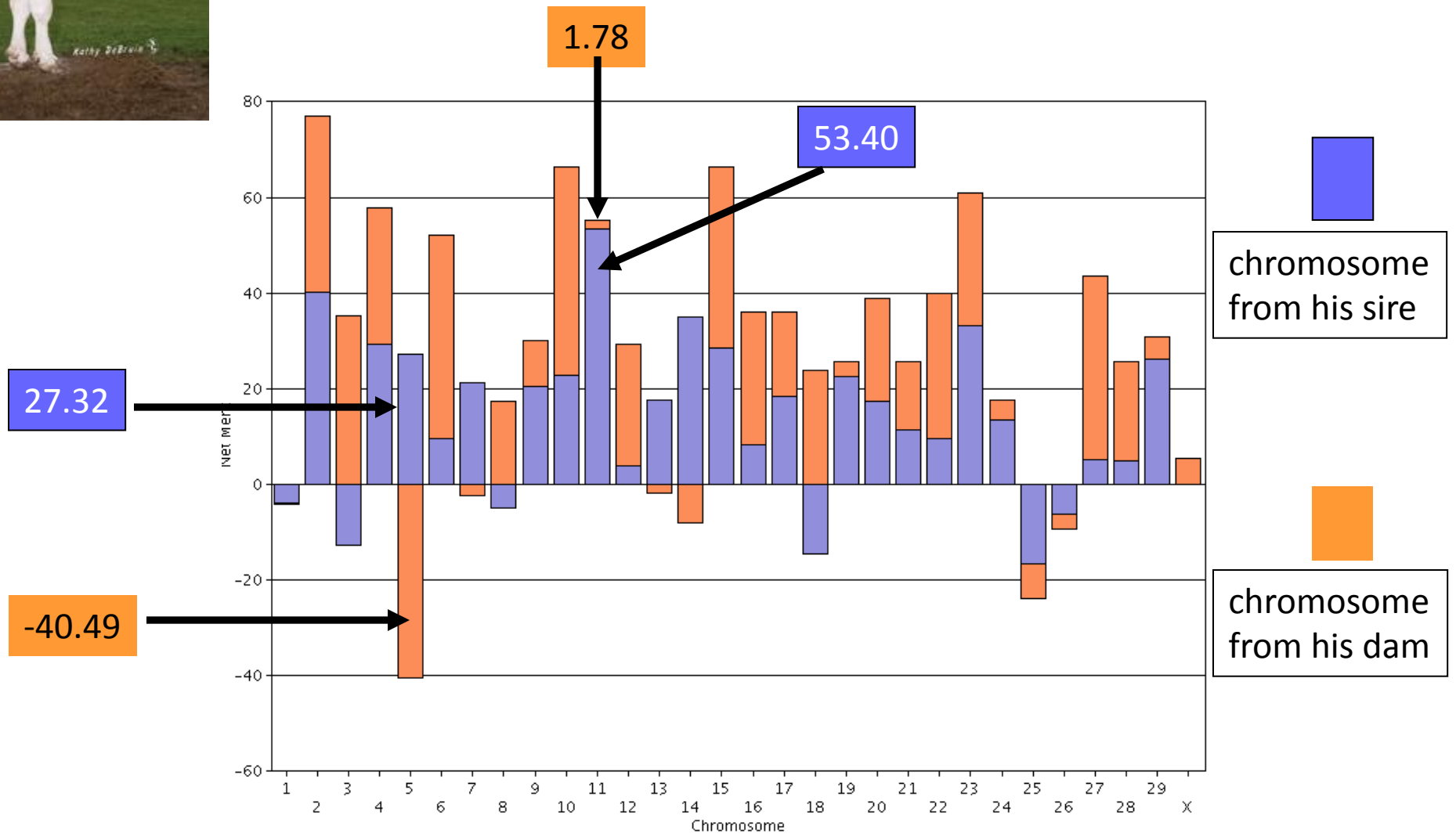
Fat Yield



Cow Conception Rate



Genomic Prediction tells us, how his genetic merit will be transmitted.



Chromosomal PTA for NM$

With Genomics:

We're able to determine if an offspring received

good *or* ***bad*** *alleles from its parents*

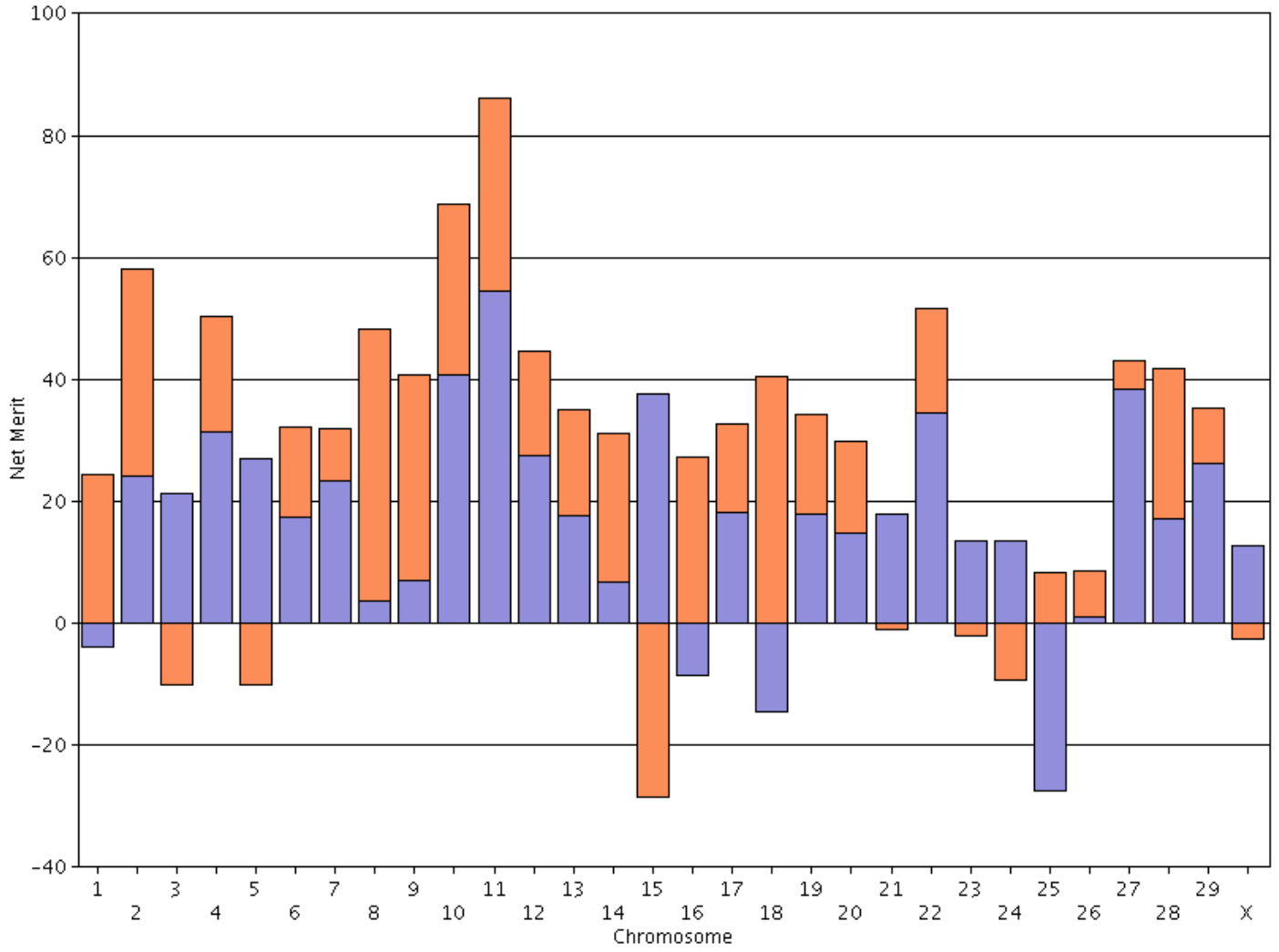
chromosome from her **sire**

chromosome from her **dam**

Polygenic: genetic variation not explained by markers

A top daughter of this bull

Net Merit	$702
Sire	$381
Dam	$296
Polygenic	$25

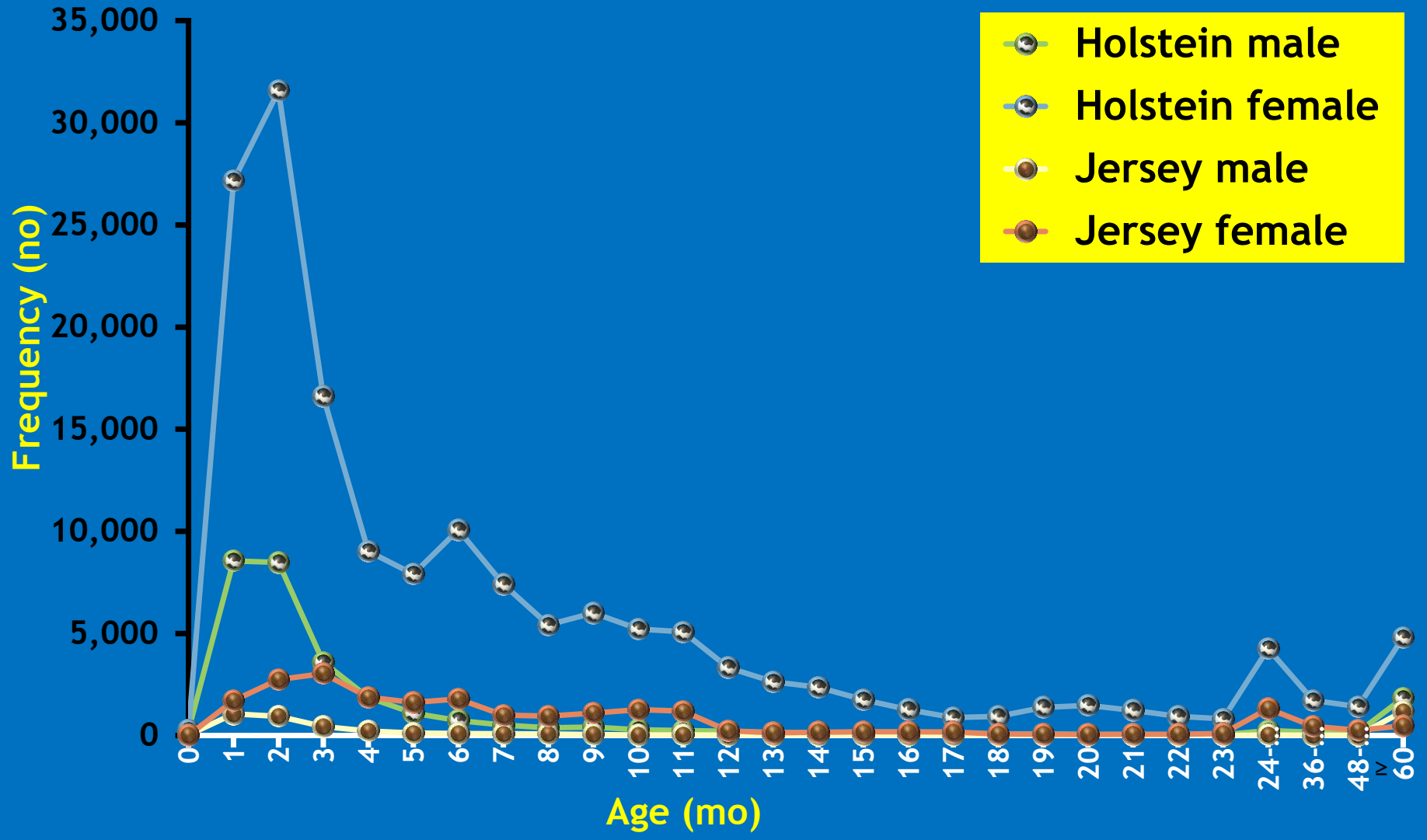


chromosome from her **sire**

chromosome from her **dam**

Polygenic: genetic variation not explained by markers

Most animals are being tested at less than 4 months of age



Two main reasons

- Selection of superior breeding stock - elite animals
- Early identification of animals that should be culled.

Genetic Gain per Year

$$\Delta g = \frac{ri\sigma}{L}$$

$$\frac{\text{(Accuracy x Intensity x Genetic Variation)}}{\text{Generation Interval}}$$

What we want to do.

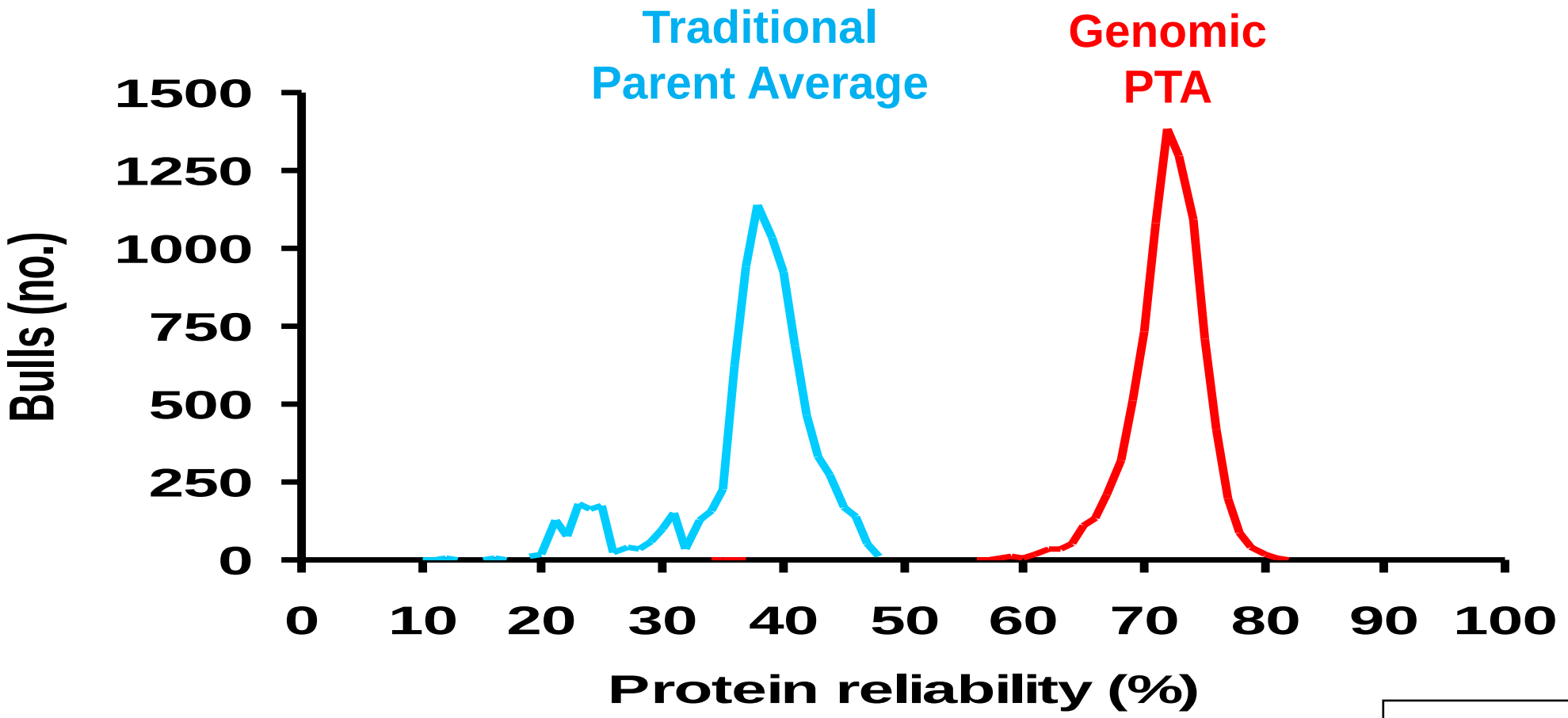
↑ **Accuracy by using genotypic data**

↑ **Select more intensely**

↓ **Generation interval by obtaining evaluations earlier in life**

A genomic test gives you a more accurate prediction of genetic merit

Reliabilities for Young Animals

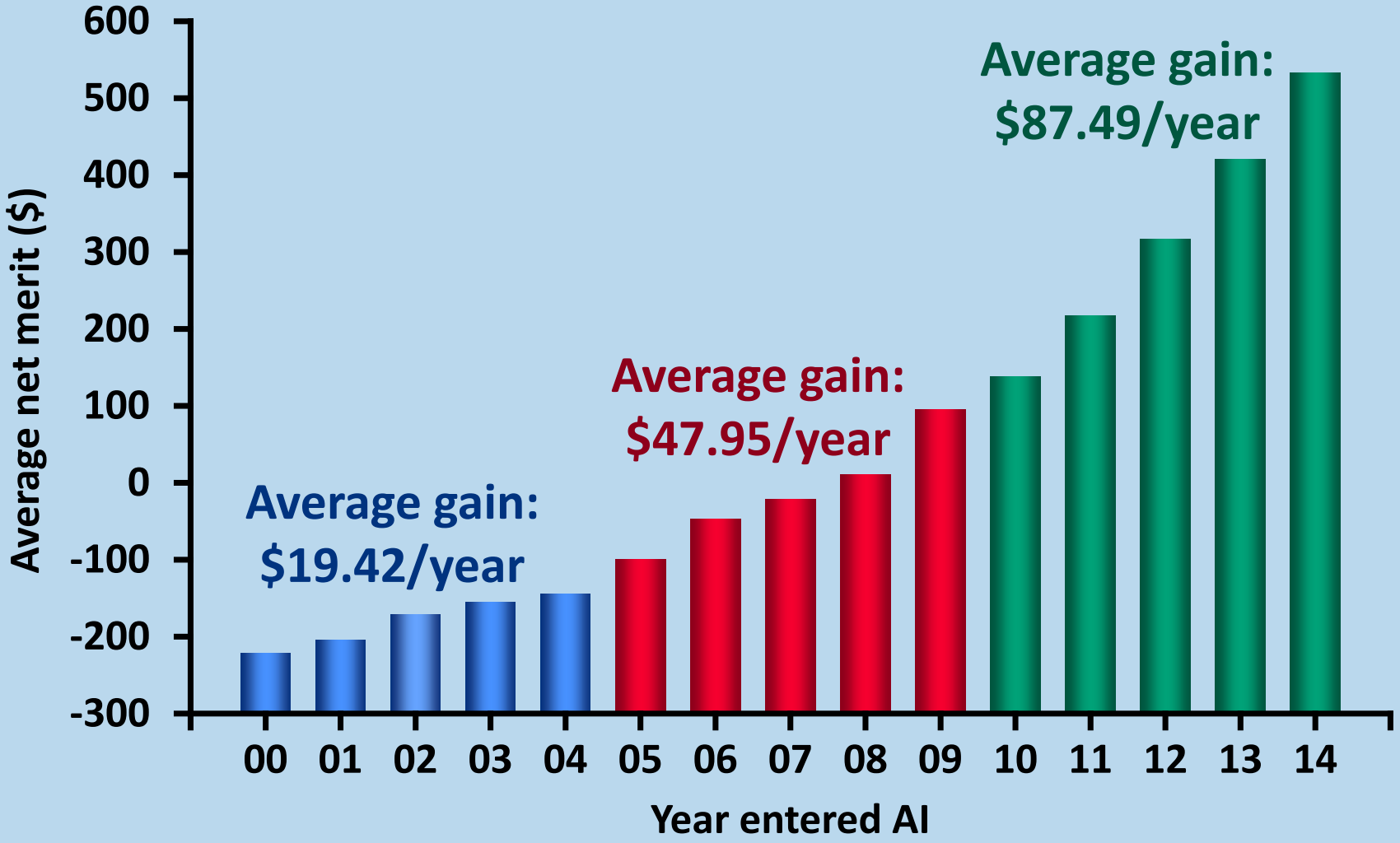


Accuracy = $\sqrt{\text{reliability}}$

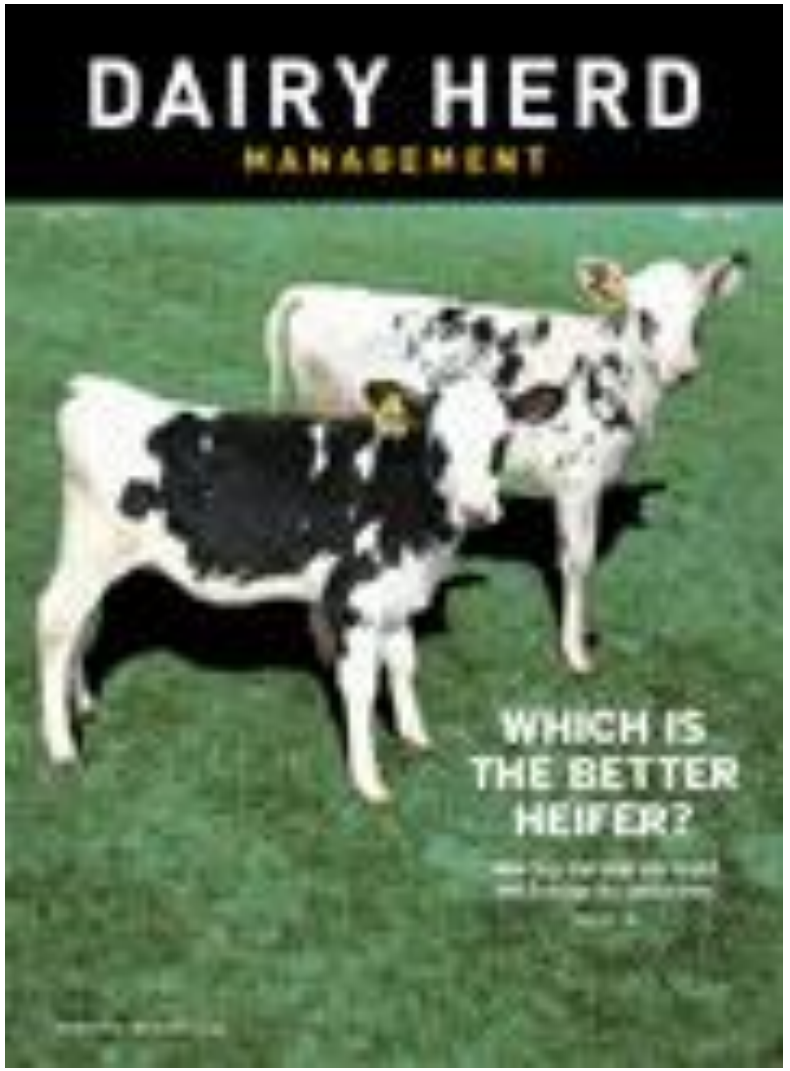
Generation Interval

Age of **Parents** when he was born	Age of **Grand Parents** when his parents were born	Age of **Great Grand Parents** when Grand Parents were born	Age of **Great Great Grand Parents** when Great Grand Parents were born
20 months	**22.5** months	**33.8** months	**62.1** months

Genetic merit of marketed Holstein bulls
improving at a faster rate



Better Herd Management

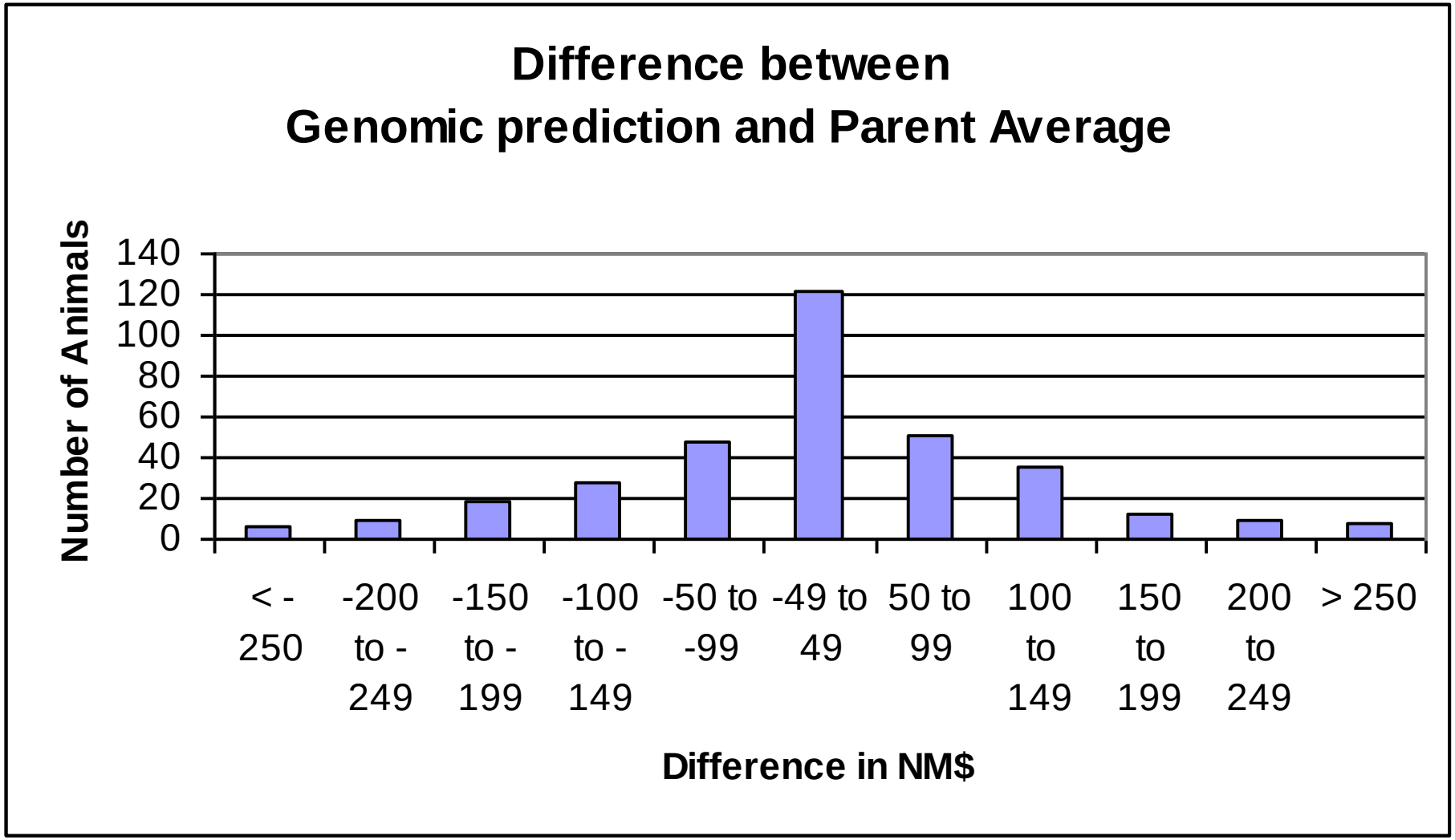


Heifer selection with genomic testing

"We have to continually ask ourselves, 'How can we become more efficient?' 'How can we maximize profits?' and 'How can we improve the quality of our animals?'"

Chaput Family Farms, North Troy, Vt.

Early identification of elite animals and ones that should be culled or bred to a beef bull.



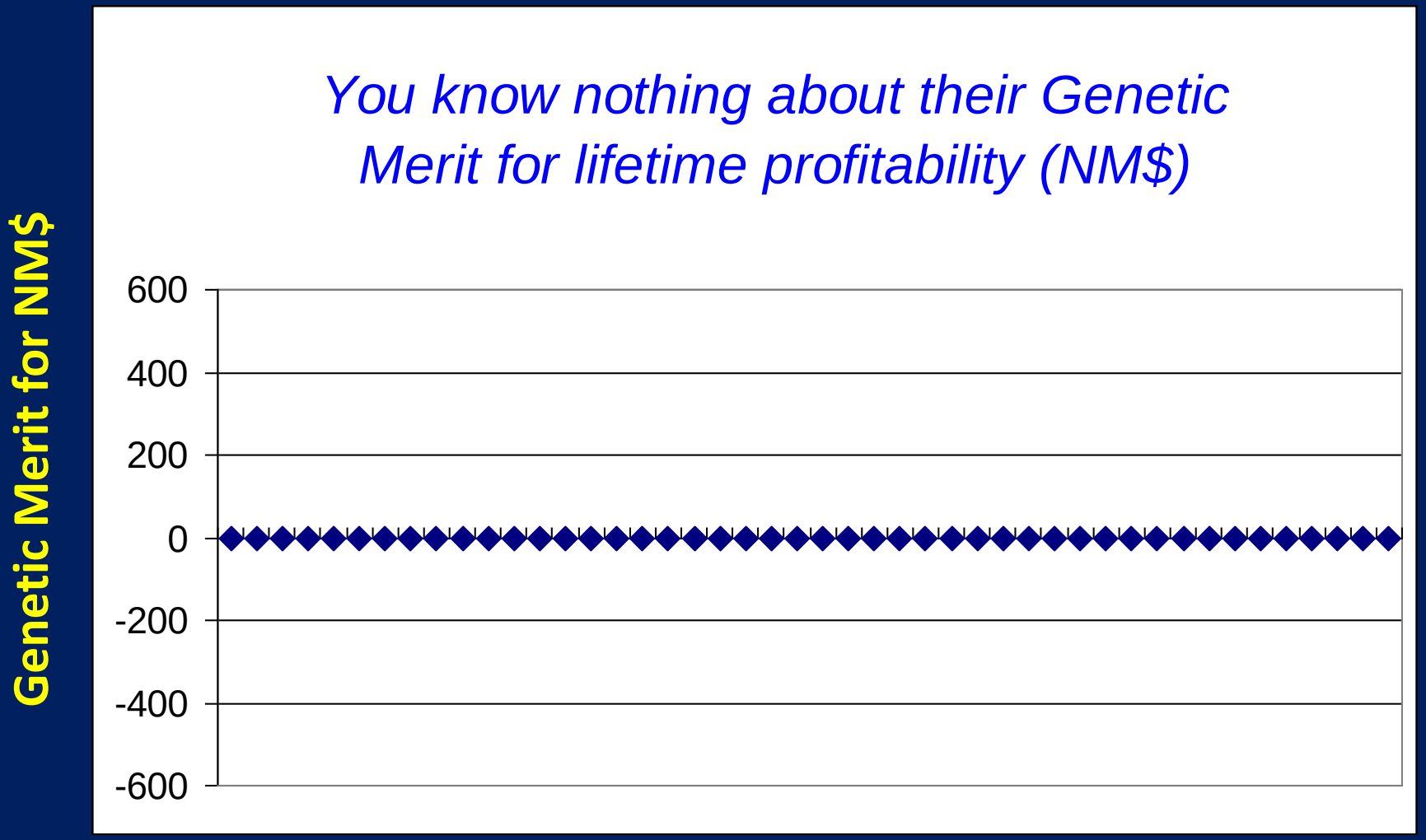
Welcome Stock Farm - *Schuylerville, NY*

Example of 1 days worth of DNA samples from 1 large commercial farm

Source: Paul VanRaden, USDA

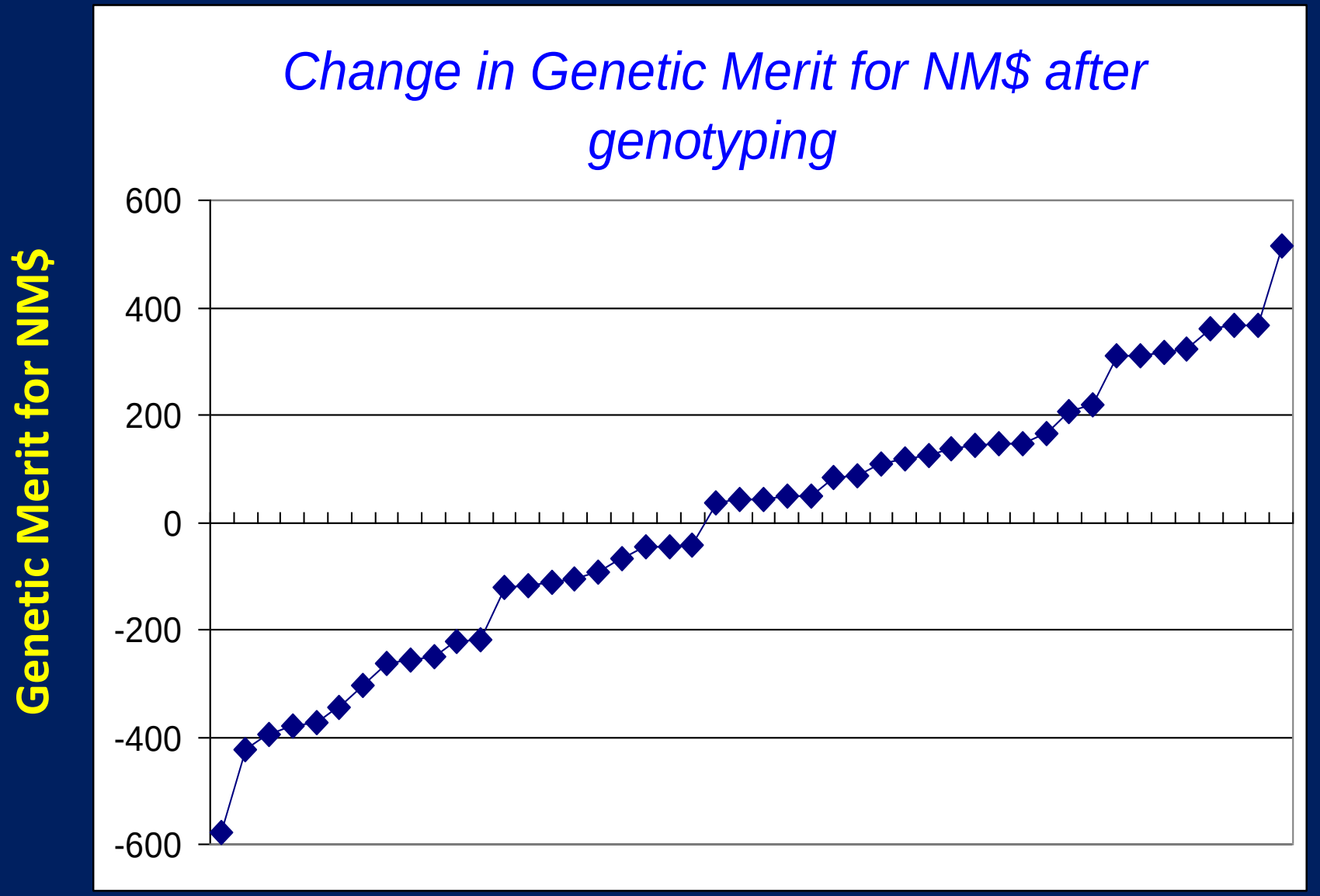
Photo provided by Zoetis

46 US Holsteins – unknown parents

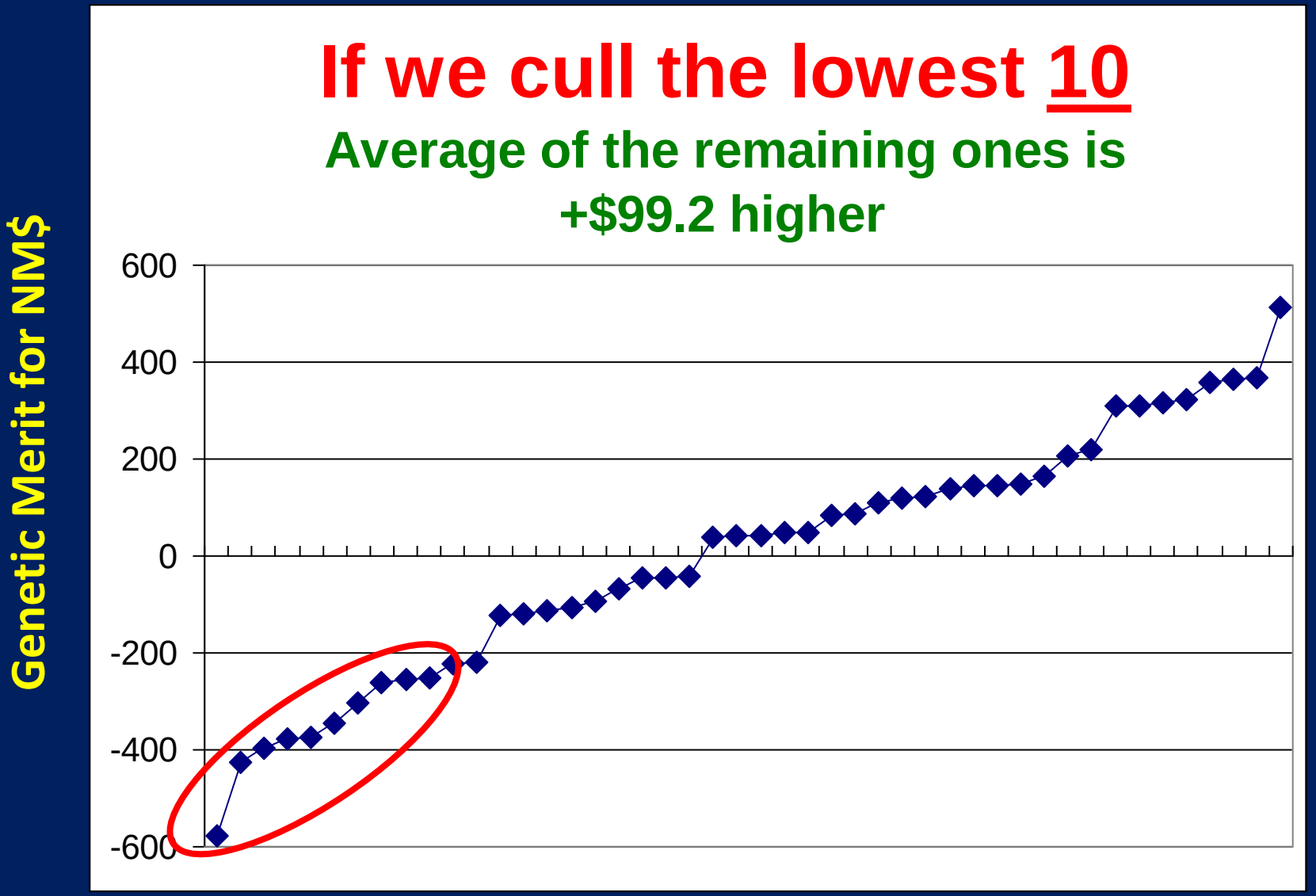


Without any pedigree information, they all appear the same!

46 US Holsteins – genotyped



The poorest animals can be culled



Study done by University of Wisconsin

Genomic predictions are much more accurate than just using the Sire's PTA.

Leading to more accurate culling decision.

Table 2. First lactation ME 305-day milk yield based on sire's PTA milk

Quartile	Number of cows	Average sire PTA milk (lbs.)	Actual ME 305-day milk yield (lbs.)
Top 25%	103	1,780	29,864
Top 25-50%	103	1,168	29,673
Bottom 25-50%	103	762	29,247
Bottom 25%	102	128	27,498

Spread
29,864
– 27,498
= 2366

Table 1. First lactation ME 305-day milk yield based on genomic PTA milk

Quartile	Number of cows	Average genomic PTA milk (lbs.)	Actual ME 305-day milk yield (lbs.)
Top 25%	103	1,358	31,581
Top 25-50%	103	832	30,050
Bottom 25-50%	103	482	27,864
Bottom 25%	102	-57	26,780

Spread
31,581
– 26,780
= 4801
pounds
of milk

Genomic testing allows farmers to jump ahead of the competition !

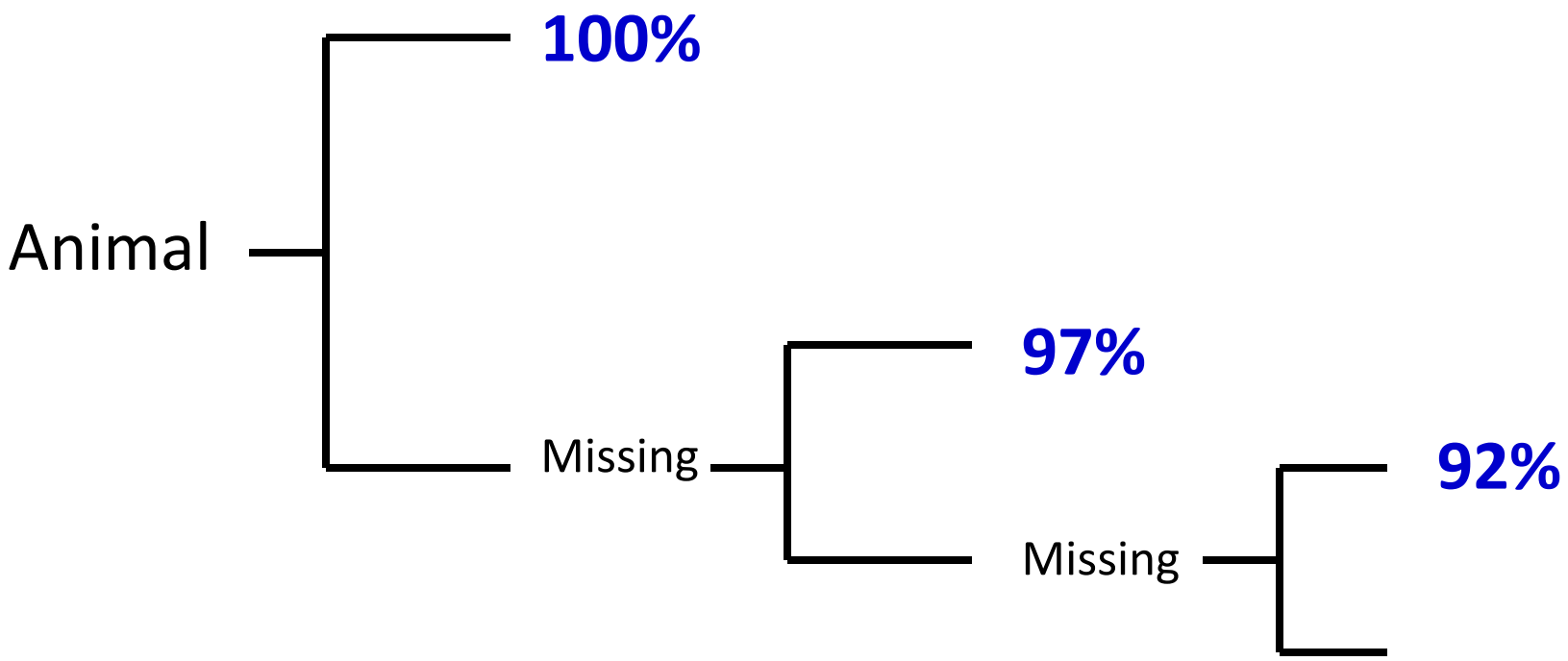
Many herds are interested in Parentage verification and discovery

Who's your daddy?

We can often identify the sire of the animal

Probability of finding a missing relative

When the bull has been genotyped.



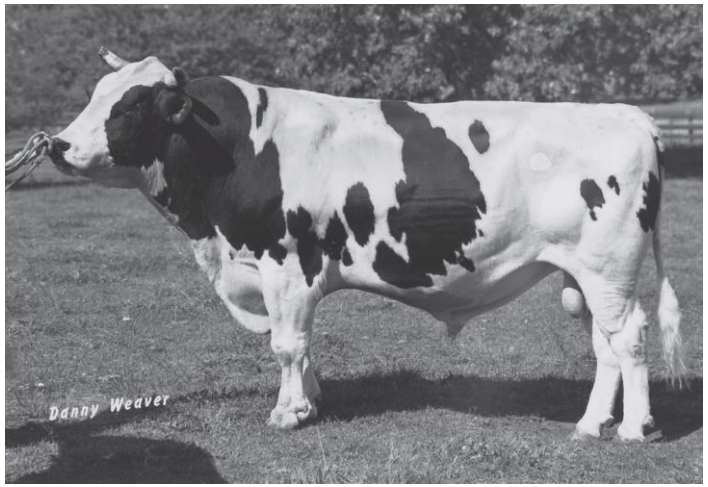
Sire can be verified
Confirmed, Corrected or Discovered

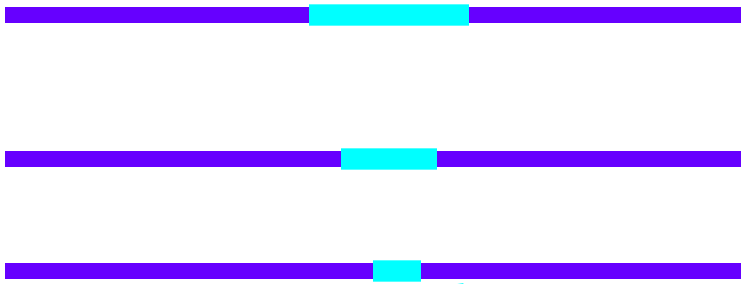
	Verified	Not Found
North America	95.8	4.2
Western Europe	91.9	8.1
Eastern Europe	90.7	9.3
Oceania	73.2	26.8
Latin America	77.8	22.2
Asia	71.4	28.6
Africa	95.6	4.4

Source: USDA-CDCB

New molecular tools are helping us identify the effect of single genes.

- As more animals are genotyped, new crossovers occur, which allows us to narrow down the affected DNA area segment.
- Mapping the defect to a small section of DNA.





part of the original chromosome

Use sequence data to find causative mutation

HH1 – Holstein Haplotype 1

- Exact mutation found.

  CGA → arginine

  TGA → stop making this protein

- APAF1 gene is important for normal embryonic development *(apotosis).*

- HH1 is a Loss-of-Function mutation and it's lethal.

AIP RESEARCH REPORT
GENOMIC3 (09-13)
Updated Mar. 23, 2015

Haplotype tests for recessive disorders that affect fertility and other traits

J.B. Cole, P.M. VanRaden, D.J. Null, J.L. Hutchison, T.A. Cooper, and S.M. Hubbard
Animal Improvement Program, Animal Genomics and Improvement Laboratory, Agricultural Research Service, USDA, Beltsville, MD 20705-2350
301-504-8334 (voice) ~ 301-504-8092 (fax) ~ john.cole@ars.usda.gov ~ http://aipl.arsusda.gov/

http://aipl.arsusda.gov/reference/recessive_haplotypes_ARR-G3.html

One in five animals are expected to be a carrier of a genetic defect causing early embryonic loss.

VanRaden and Miller, 2006

Breed	Haplotype	OMIA 9913 ID[1]	Functional/ *gene* name	Frequency (%)	Chromosome	Region (bp)	Reference
Holstein	HBR	001199	Black/red coat color/ *MC1R(MSHR)*	0.8	18	14,757,332 – 14,759,082	Lawlor et al. (2014)
	HDR	001529	Dominant red coat color	0.04	3	9,479,761	Lawlor et al. (2014), Capitan et al. (2014)
	HH0	000151	Brachyspina/*FANCI*	2.76	21	21,184,869 – 21,188,198	Agerholm et al. (2006), Charlier et al. (2012)
	HH1	000001	*APAF1*	1.92	5	63,150,400	Adams et al. (2012)
	HH2	001823	—	1.66	1	94,860,836 – 96,553,339	VanRaden et al. (2011), McClure et al. (2014)
	HH3	001824	*SMC2*	2.95	8	95,410,507	Daetwyler et al. (2014), McClure et al. (2014)
	HH4	001826	*GART*	0.37	1	1,277,227	Fritz et al. (2013)
	HH5	001941	—	2.22	9	92,350,052 – 93,910,957	Cooper et al. (2013)
	HHB	000595	BLAD/*ITGB2*	0.25	1	145,119,004	Shuster et al. (1992)
	HHC	001340	CVM/*SLC35A3*	1.37	3	43,411,473	Agerholm et al. (2001)
	HHD	000262	DUMPS/*UMPS*	0.01	1	69,757,801	Shanks et al. (1984)
	HHM	000963	Mulefoot/*LRP4*	0.07	15	77,663,790 – 77,701,209	Eldridge et al. (1951), Duchesne et al. (2006)
	HHP	000483	Polledness/*POLLED*	0.71	1	1,705,834– 1,989,480	Medugorac et al. (2012), Rothammer et al. (2014)
	HHR	001199	Red coat color/ *MC1R(MSHR)*	5.42	18	14,758,207	Joerg et al. (1996)

Mating Programs
are used to prevent carrier to carrier matings

Recessives To Exclude:

- [ ] BL - BLAD
- [ ] BY - Brachyspina
- [ ] CV - CVM
- [ ] MF - Mule-Foot

Haplotypes To Exclude:

- [x] **Exclude**

- [x] HH1
- [x] HH2
- [x] HH3

RED BOOK+ MultiMate Plus

Male Carriers for Haplotypes Impacting Fertility on the Records of Holstein Association USA, Inc. as of 08/11/2015
(Blank=Tested-Free, C=Carrier) Use CTRL-F to search.

Stud Code	Name	Registration	HH1	HH2	HH3	HH4	HH5	HCD
	REDAMA LINOT-ET	CAN 101242905						
73HO01950	REDAMA LOUGANO-ET	CAN 5553151	C					
200HO04197	REDAMA LUIGI-ET	CAN 6929629						
	REDAMA NAPOLITIAN-ET	CAN 8294735						
200HO05370	REDAMA RIVIERA-ET	CAN 102476028						
	REDCARPET AERO CHILL-ET	USA 72530625						
	REDCARPET ALCHEMY SKYRIM	USA 72189767						
	REDCARPET BATLEOFBRITAIN-ET	USA 72203392						3
	REDCARPET BOLO BOSTON	USA 71495757						
	REDCARPET CLT ZINFANDEL-RED	USA 71743673						
	REDCARPET DREADNOUGHT-ET	USA 72189830						1
	REDROCK-VIEW MCHUTCHEN 401	840003128204849						
198HO01998	REDSILK-RED	DEU 357167914						1
200HO08077	REDSTAR VISCOUNT-IMP-ET-RED	AUS 1387193						
	REDSTIEN BURST CAMEL-RED	USA 143082231		C				

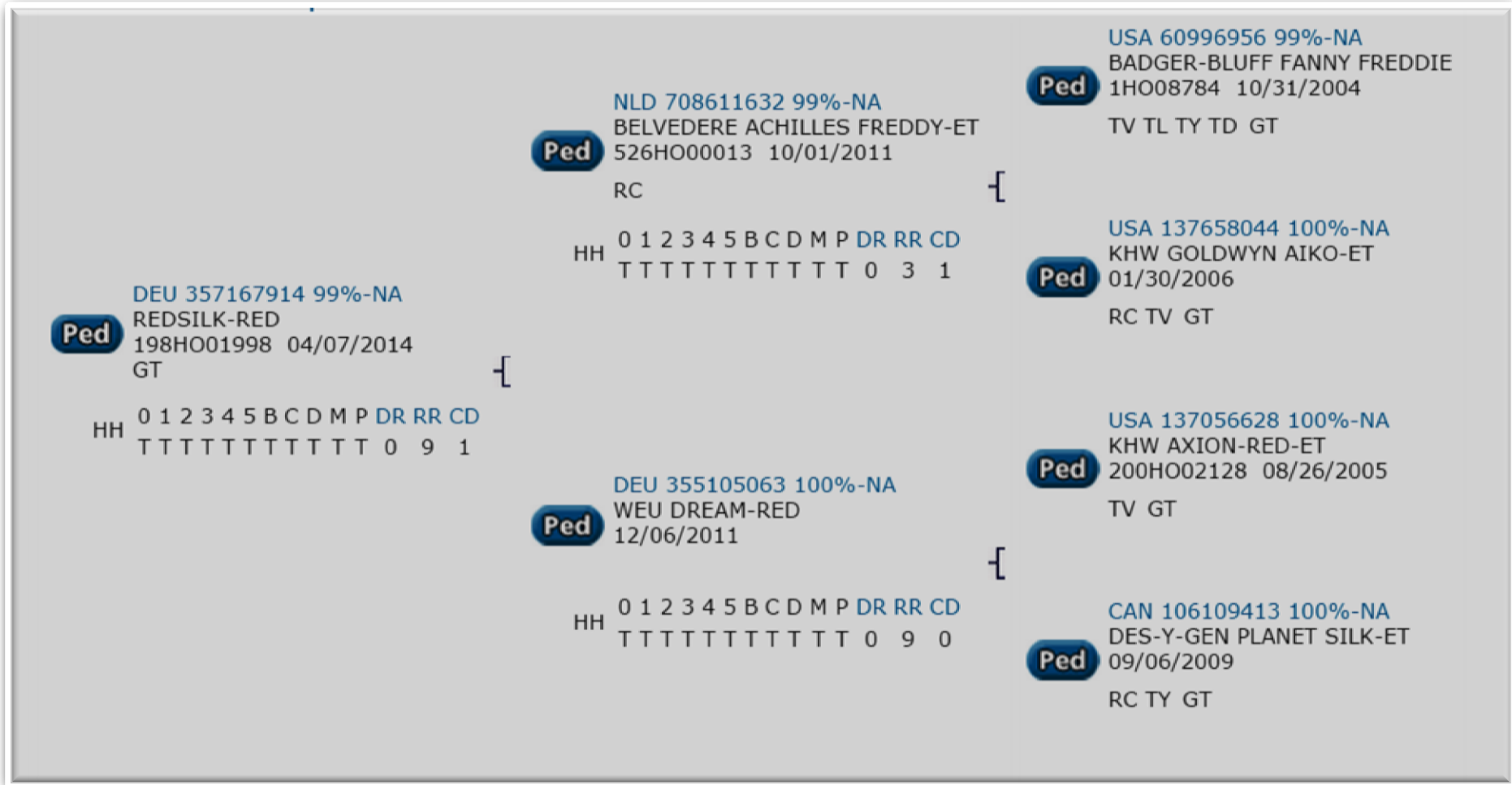
Family Tree

free lookup on www.holsteinusa.com

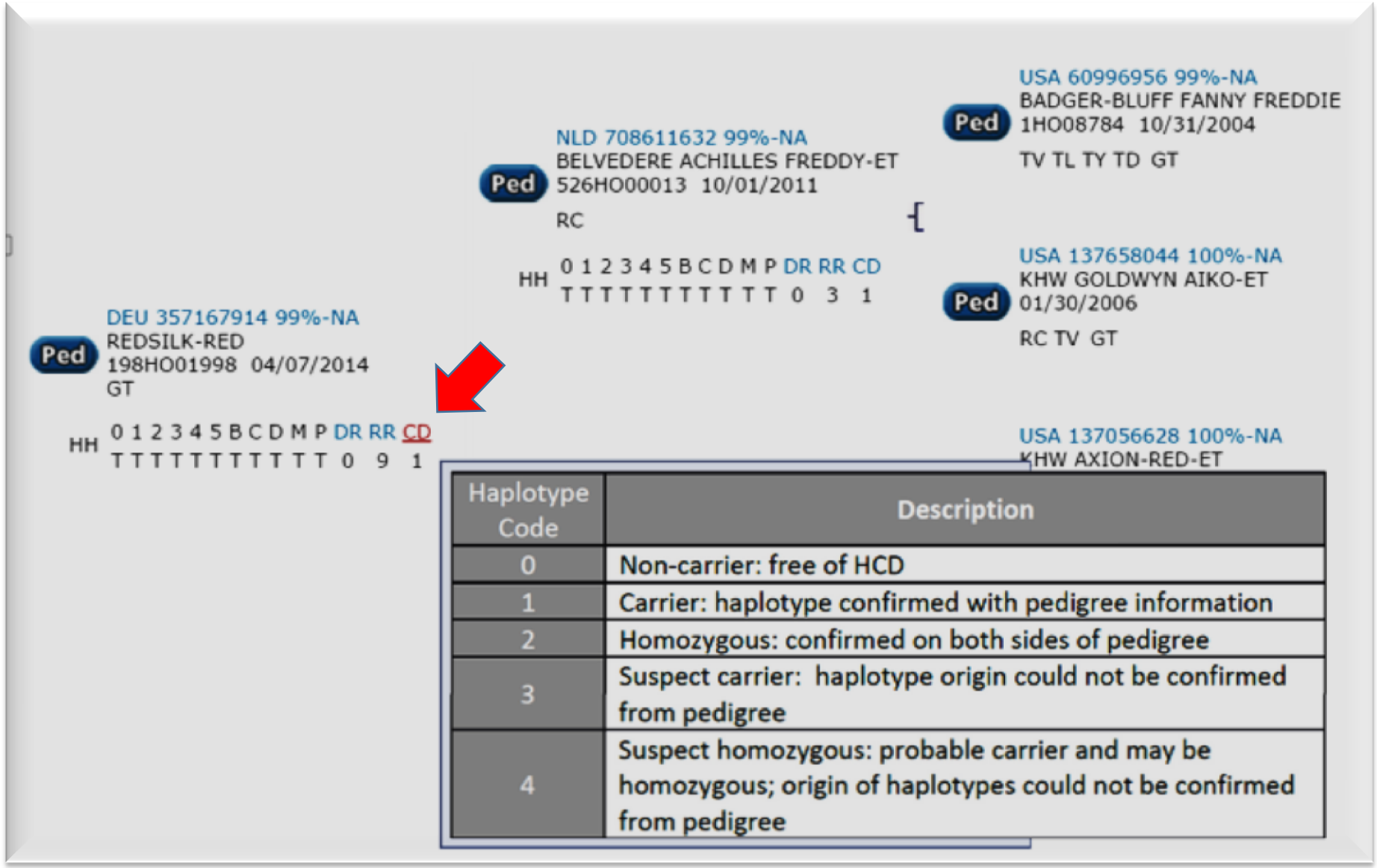
HCD

New undesirable genetic condition

Haplotype associated with **C**holesterol **D**eficiency



To obtain explanation of haplotype codes
Move **cursor** over Code

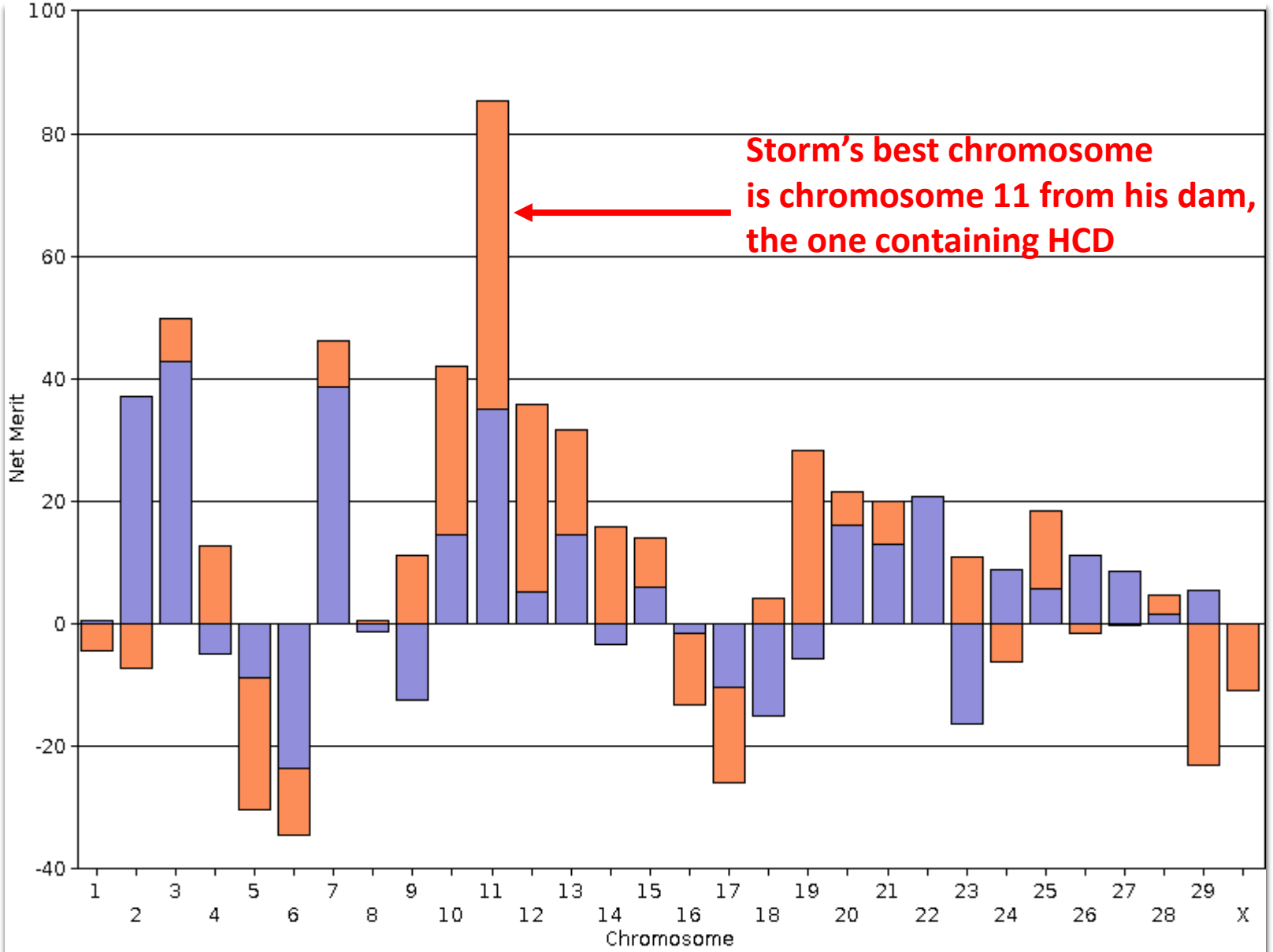


Haplotype Code	Description
0	Non-carrier: free of HCD
1	Carrier: haplotype confirmed with pedigree information
2	Homozygous: confirmed on both sides of pedigree
3	Suspect carrier: haplotype origin could not be confirmed from pedigree
4	Suspect homozygous: probable carrier and may be homozygous; origin of haplotypes could not be confirmed from pedigree

Identification and Management of Deleterious Mutations

- New molecular tools has made it easier to identify and manage undesirable genetic characteristics.
- We no longer eliminate superior animals that have an undesirable genetic conditions.
- We use breeding tools to avoid carrier to carrier matings.
- Each generation - selective breeding and testing is used to lower their frequency.

Undesirable haplotypes increase in frequency because they're usually connected to a number of desirable alleles



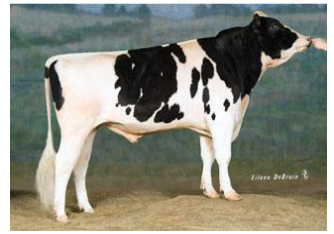
HCD

New undesirable genetic condition

Haplotype associated with
Cholesterol
Deficiency

Lowering the rate of increase in inbreeding

- With any fast improving selection program, we are going to see an increase in inbreeding as we bring the better genes in the population together.



- We especially see this within the mating of the most elite animals

- It's recommended that you choose amongst 5 elite bulls and make a balanced decision between the TPI-adjusted for inbreeding and the actual genomic inbreeding value listed.

Inbreeding Calculator

USING THE INBREEDING CALCULATOR

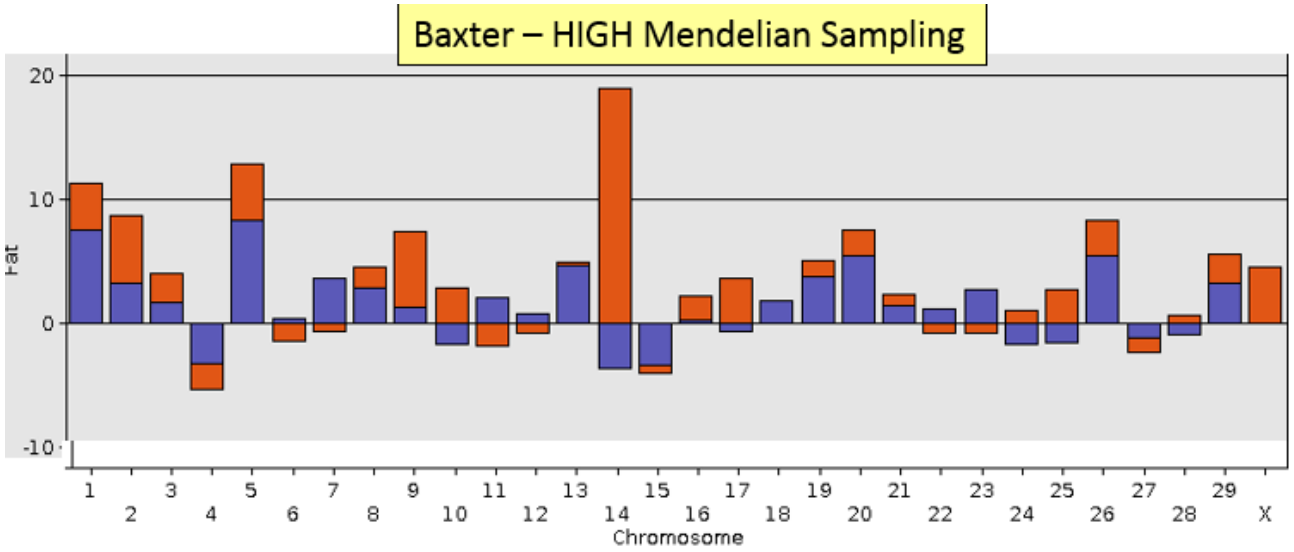
(in descending order from highest adjusted TPI)

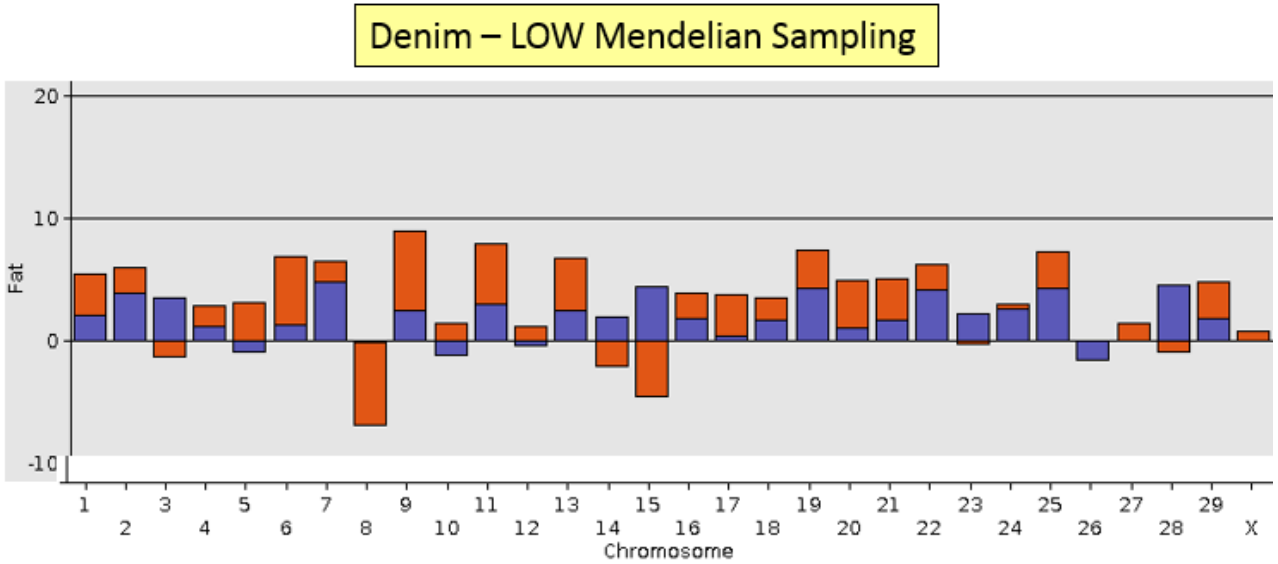
Dam: USA 71541106 COOK-FARM UNO HAIZE

Sire		Inbreeding % Pedigree	Genomic
USA 71753166	RIVER-BRIDGE CO-OP TROY-ET	5.5 %	9.9%
NAAB: 1 HO 11056 (TROY)			
Parent Averages			
Parent Averages Adjusted for Inbreeding			

Sire		Inbreeding % Pedigree	Genomic
CAN 11596146	STANTONS MAIN EVENT-ET	6.7 %	12.2%
NAAB: 250 HO 1127 (MAIN EVENT)			
Parent Averages			
Parent Averages Adjusted for Inbreeding			

Other applications



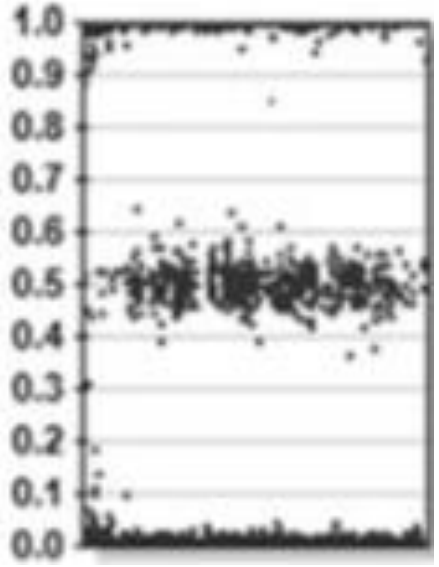


Baxter has more extreme daughters

PTA Fat	Denim	Baxter
> 75 lbs	5%	**9%**
20 to 75	92%	82%
< 20 lbs	3%	**9%**

Genetic explanation of unusual phenotypes.

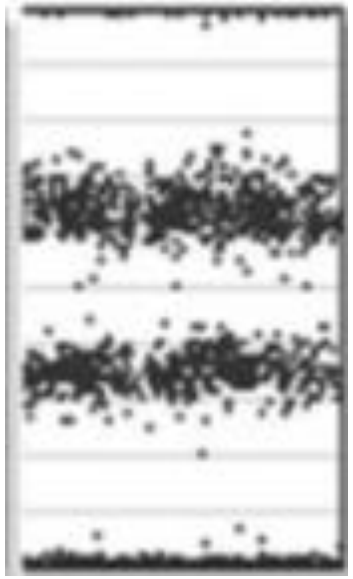
Test for chimera



BB

AB

AA



Cells from ONE embryo

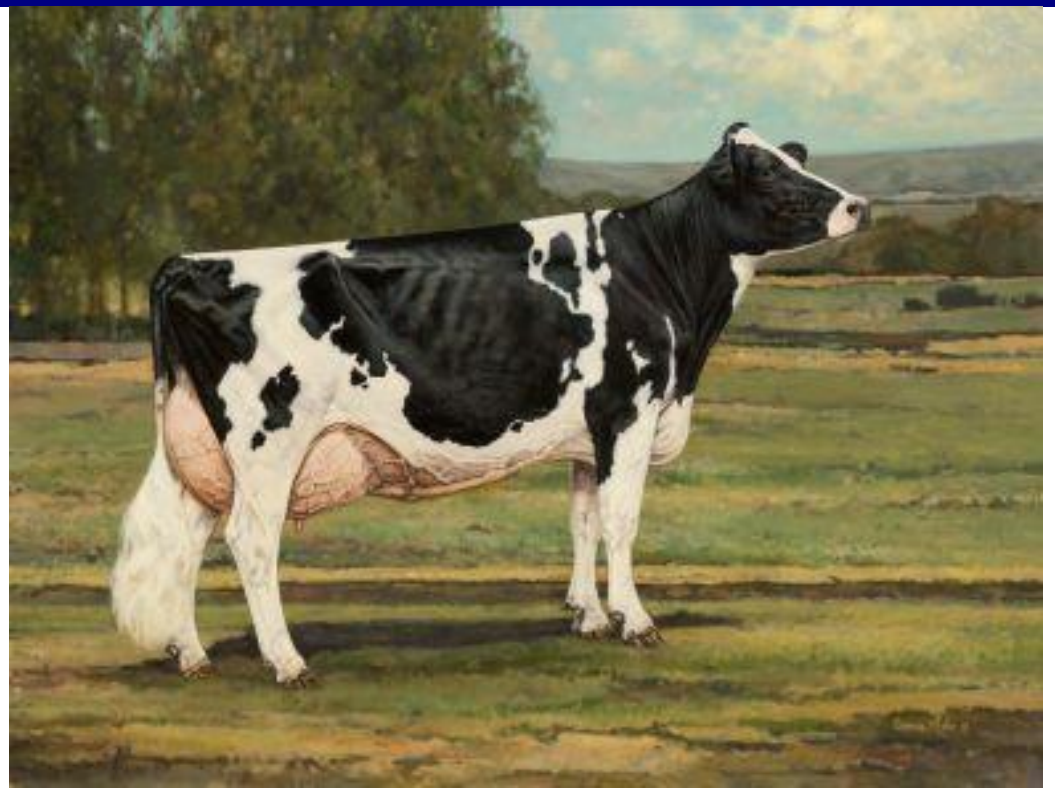
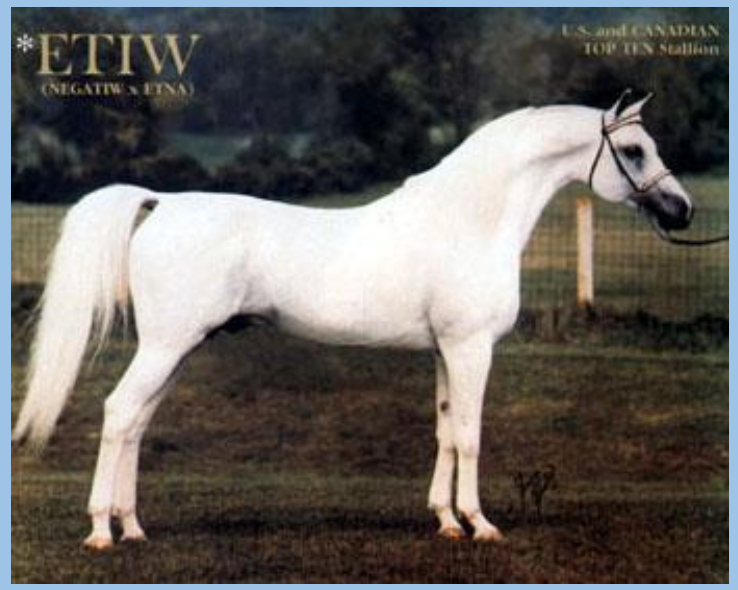
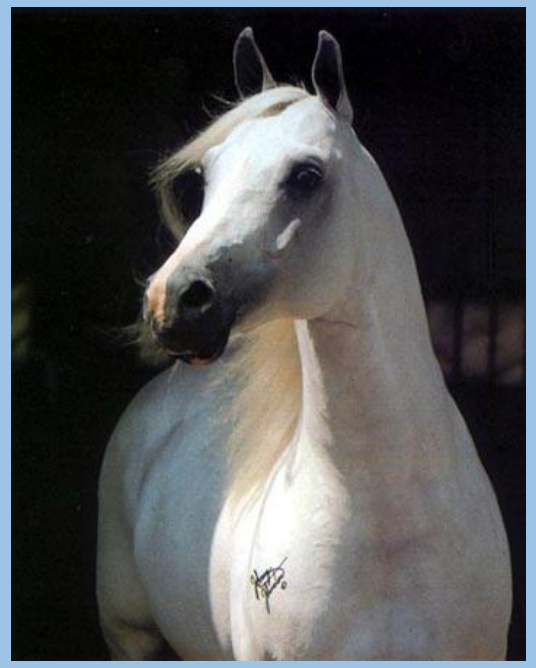
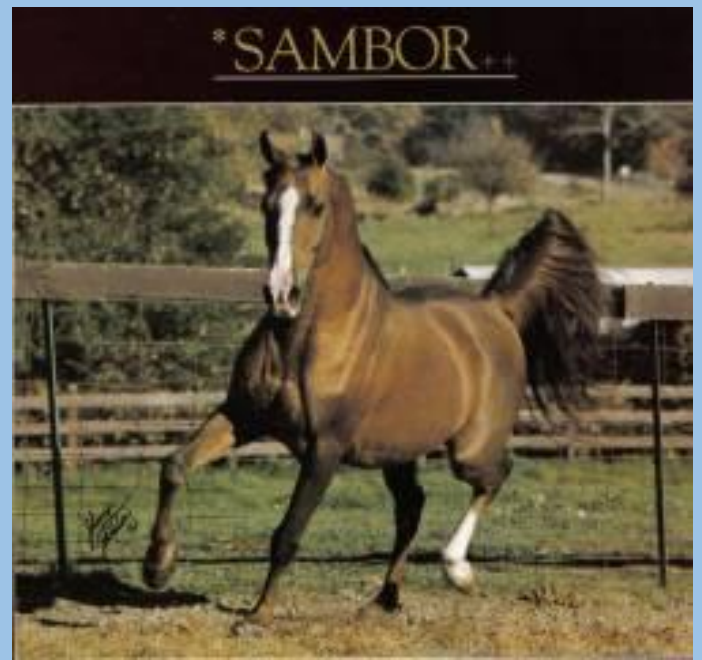
Cells from TWO embryos

Gene for Dilution of black coat color ?

Genomic information is being used in many ways within the U.S. dairy industry.

Sparking a renewed interest in genetics

Any questions ?



My early experience with fine Polish breeding animals