

# Introduction to Genomic Selection

Minnesota Dairy Health Conference



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Like vaccination, and segregation, a genetic approach to improve health is a type of preventative measure. Genetic improvement to improve health is a long-term process but elicits permanent gains as genetic gains made in one generation remain in future generations under a program of continued selection. This talk explores the opportunities and challenges of host genomic approaches to reducing the prevalence of disease and improving animal health.

## OUTLINE



1. What is different between pedigree based and genomic selection?
2. Selection tools
  - Selection Indexes
  - Genotyping resources
3. DNA-based markers and their use in dairy breeding programs



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## WHY USE SELECTION?

Estimated cost to raise a heifer is \$2000-\$3000

To improve performance

- Nutrition
- Hygiene
- Health program
- Genetics ← **Selection**



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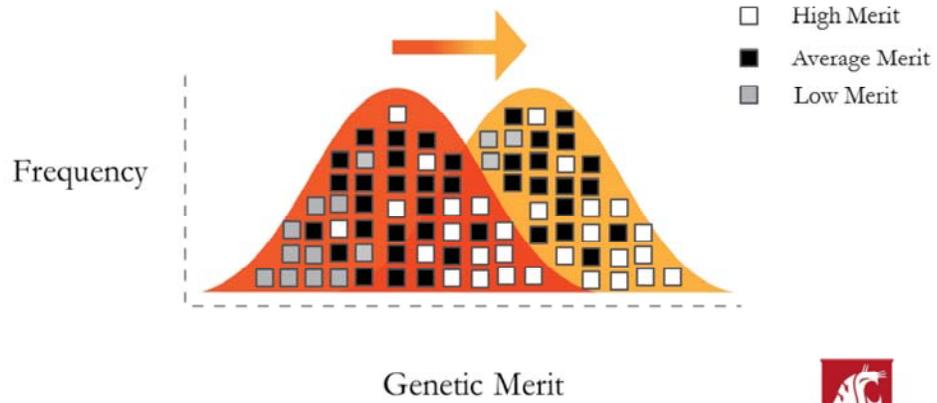
## ACHIEVEMENT OF GENETIC CHANGE IN RESPONSE TO SELECTION

$$\text{Genetic Change} = \frac{\text{Accuracy of selection} \times \text{Selection intensity} \times \text{Genetic variation}}{\text{Generation Interval}}$$



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# EFFECT OF ACCURACY (RELIABILITY)



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## ACCURACY (RELIABILITY)

Accuracy depends on:

- Amount and type of information available
- With phenotypic selection, high accuracy occurs with high heritability
- Improving accuracy improves the response to selection
- In the dairy industry the term reliability ( $\% r$ ) is often used for accuracy



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Accuracy is different with information from genomic predictions compared to causal variants

Accuracy improves with more information and information from progeny. For example, a newborn calf with parental information only will have an accuracy or reliability of 42%. If that same calf is genomically tested the reliability increases to 65% and if 300 progeny are included into the evaluation, then the reliability is 96%. This allows the breeders to be more confident in the prediction of this animal's value.

## SELECTION INTENSITY



How high the threshold is for animals that will be used in the breeding population

- High selection intensity increases the rate of response to selection



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## GENERATION INTERVAL

- The average age of the parent when their offspring are born
- Reducing the generation interval through assisted reproductive technologies or genomics increases the response to selection



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Currently, 5 generations of a single sire are listed concurrently in a AI catalog – generation intervals have dropped dramatically in the AI industry.

## SELECTION PEDIGREE-BASED PTA

### **Predicted Transmitting Ability (PTA)**

- Estimates (predicts) the future offspring's performance based on records obtained from:
  - Own performance
  - Relative's performance (pedigree)
  - Past offspring's performance
- Accuracy of prediction is typically poor until a large number of progeny have performance records



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## SELECTION PREDICTION EQUATIONS

The PTA measures the expected difference between the animal's offspring and the mean of all offspring for that trait.



mean of the herd's offspring = 25,000 pounds

mean of the cow's offspring = 27,000 pounds

PTA = +2000 lbs.



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## SELECTION PEDIGREE-BASED PTA

### Pros

- Very effective with animals with large numbers of progeny
- Most effective with traits that are:
  - Easy to measure
  - Inexpensive to measure
  - Occur early in life
  - Moderate to high heritability



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## SELECTION PEDIGREE-BASED PTA

### Cons

- Accuracy is low for most females throughout their lives
- Expensive and time consuming to “prove” bulls through extensive progeny testing
- Not effective for traits that are:
  - Difficult to measure
  - Expensive to measure
  - Occur late in life



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## SELECTION GENOMIC BASED PTA

Use pedigree information **AND** information from thousands of DNA variants to predict performance of offspring

### Cons

- If the DNA variant isn't causal, prediction may not be accurate across breeds and will need to be routinely validated



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## GENOMIC SELECTION

### Pros

- Prediction can be immediate (birth) rather than waiting for offspring to perform
- Best value when:
  - Selecting for traits that are difficult to measure
  - Selecting for traits that are expensive to measure
  - Selecting for traits that occur late in life
  - Animal has 0 or few offspring



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# IMPROVING ACCURACY



Trait	Reliability%				
	Genomic Average	Traditional Parent Average	Difference Young Holstein Bulls <sup>1</sup>	2013 Difference Holstein Heifers <sup>2</sup>	Genomic Daughter Equivalents <sup>2</sup>
Net Merit (\$)	75	33	+ 42	+42	33.1
Milk (pounds)	78	35	+ 43	+44	26.6
Fat (pounds)	78	35	+ 43	+44	26.6
Protein (pounds)	78	36	+ 42	+44	26.6
Productive Life (months)	73	29	+ 44	+43	77.6
Somatic Cell Score	75	31	+ 44	+43	58.5
Daughter Pregnancy Rate (%)	71	27	+ 43	+42	146.3
Final Score	76	32	+ 44	+46	26.8
Sire Calving Ease	73	54	+ 18	+28	39.5
Daughter Calving Ease	61	36	+ 25	+28	45.1

<sup>1</sup> Genomic minus traditional for 1909 young bulls (CDCB, 2016). <sup>2</sup> Genomic minus traditional for = 240,618 Holstein heifers (AIPL-USDA, 2013)

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## SELECTION PEDIGREE AND GENOMIC PTA

- Concepts of predicting offspring performance are the same
- New opportunities to improve prediction of offspring's performance
- Dramatically increases rate of genetic change



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# DNA

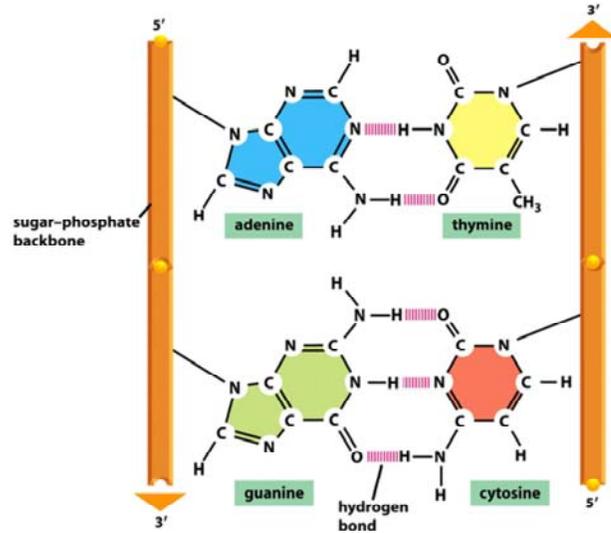
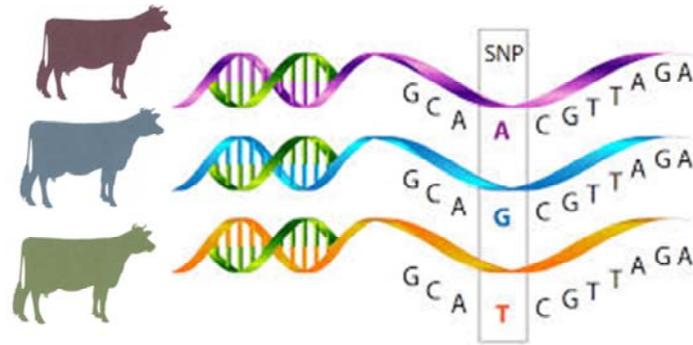


Figure 4-4 *Molecular Biology of the Cell* (© Garland Science 2008)



# SINGLE NUCLEOTIDE POLYMORPHISMS



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## GENETIC VARIATION

How much genetic variation is present in cattle?

- Single nucleotide polymorphism (SNP) is found every 70 bp and if rare SNPs are removed, one is found every 120 bp

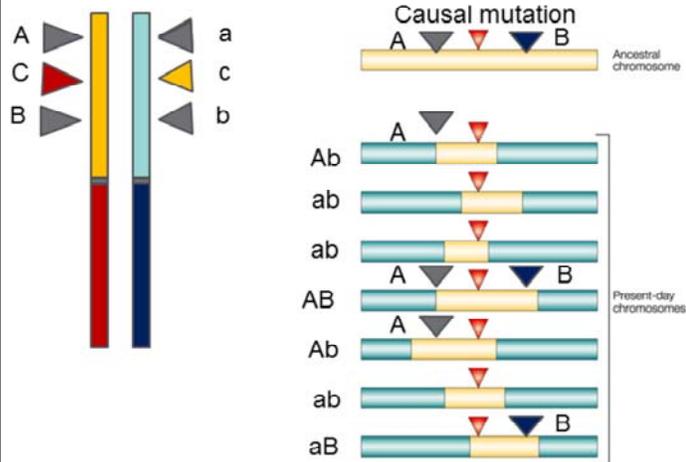
[www.broadinstitute.org](http://www.broadinstitute.org)



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In the USA, the majority of cattle affected with Johne's disease are Holsteins. Because the effective population size of the Holstein population worldwide is estimated to be less than 200, there have been concerns raised that the breed is too inbred and that this inbreeding has resulted in a lack of genetic variation. Genetic variation is critical in the ability to make genetic improvement. If the genome is identical, or nearly identical between the genomes of most cattle, then selection will not make much progress because there will be few animals with DNA that differ from one another to select from. Genotyping or analyzing the DNA at just a few regions across the genome can bias our view of how much genetic variation is present in cattle. Some regions will have a lot of variation and others less. Genomic regions under selection are especially likely to have a limited amount of variation as animals with the favored genomic variants will be in greater frequency than those with the less favorable variants. Recent efforts by the international genetics community has resulted in the whole genome sequencing (and sharing of sequence data) of many different individuals in numerous breeds. Recent sequencing efforts has shown that in whole genome sequencing of > 200 Holsteins, a single nucleotide polymorphism was identified (on average) ~ every 70 bp and when removing variants that were present less than 1% of the time, a SNP was identified approximately every 120 bp, and this doesn't account for all of the structural variants that are present. This indicates that there is sufficient genetic variation in the cattle population to use selection to our benefit.

# LINKAGE DISEQUILIBRIUM



Adapted from: [Nature Reviews | Genetics](#)

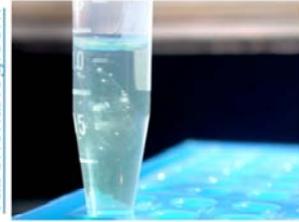
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## DNA BASED TESTS

- DNA can be extracted from any tissue including blood, hair and semen
- DNA variants are now associated with health, reproductive, and production traits

vabenefitblog.com



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## WHY ARE DAIRIES USING GENOMIC TESTS?

- Increased (and improved) reporting of traits
- Improved customer confidence in genomic tests
- Ease of access
- Cost of testing is lower
- Implementation is increasing profitability and response to selection



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Access has improved. Dairy dashboard allows the use of custom indexes based on data uploaded from genomic tests. Can upload data directly to dairy comp. Genetic advisors are assisting producers and there are specific programs to help dairy veterinarians interpret and assist dairy producers in the use of genomic information. Merck has partnered with GeneSeek (Neogen) to deliver this type of information.

Implementation – Kent Weigel’s paper on doing genomic testing and using the top heifers for ET or sexed semen, the next set of heifers use regular AI sires and the lowest heifers that are kept breed to beef AI bulls.

## Council on Dairy Cattle Breeding Genotyping Data as of 3/19/2017

Breed	Females	Males	Total
Ayrshire	5,533	1,938	7,471
Brown Swiss	6,040	25,345	20,381
Guernsey	2,400	784	3,184
Holstein	1,320,352	233,561	1,553,913
Jersey	168,425	26,258	194,683
Milking Shorthorn	15	31	46
			<b>1,790,731</b>

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## SELECTION INDEXES

- Predicted transmitting abilities (PTA) of dairy cattle are often summed into a selection index
- Selection indexes combine PTAs of various traits, weights them and gives you a single value to select by
- Weights can be based on economic value or the prioritization of what traits are the most important
- Examples: Total performance index (TPI), Net merit\$ (NM\$)

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## NET MERIT \$

The NM\$ index is defined as expected lifetime profit as compared with the breed base for cows born in 2010

Updated in 2014 to include:

- New economic weights
- 2 more fertility traits - heifer conception rate (HCR) and cow conception rate CCR)
- Grazing merit (GM\$)
- Cheese merit (CM\$)
- Fluid merit (FM\$)
- Details may be found at <http://aipl.arsusda.gov/reference/nmcalc-2014.htm>

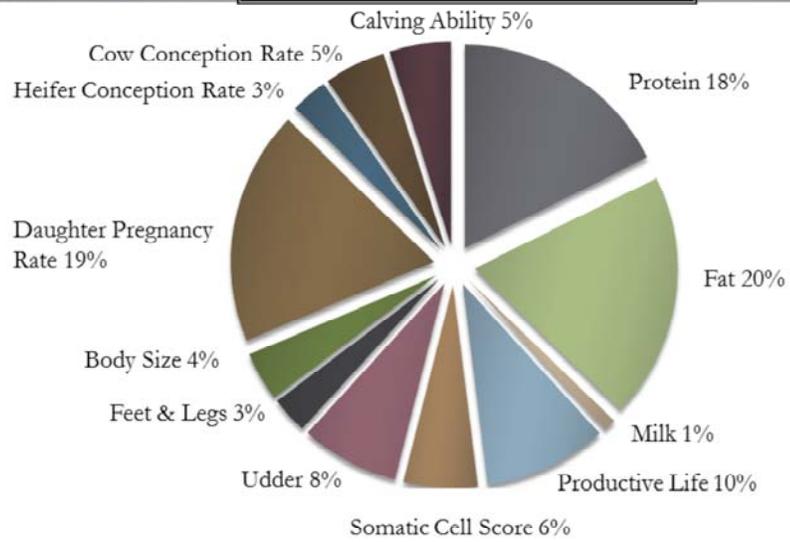
Estimated that \$8 million/year would be gained if all dairy breeders selected breeding stock using NM\$ (VanRaden and Cole, 2014)



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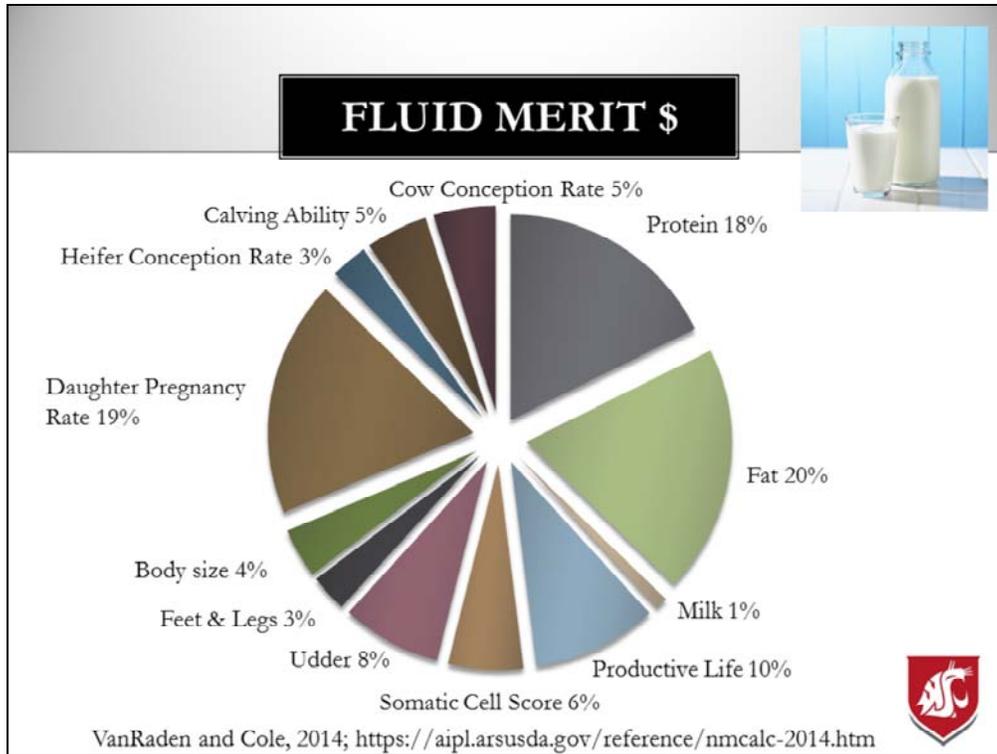
Heifer conception rate – for each 1% increase in HCR should decrease age at first calving by 0.54 days. Number of services were assumed to average 1.8 for heifers and 2.9/lactation for cows which is equivalent to conception rates of 56% and 34%, respectively

## NET MERIT \$



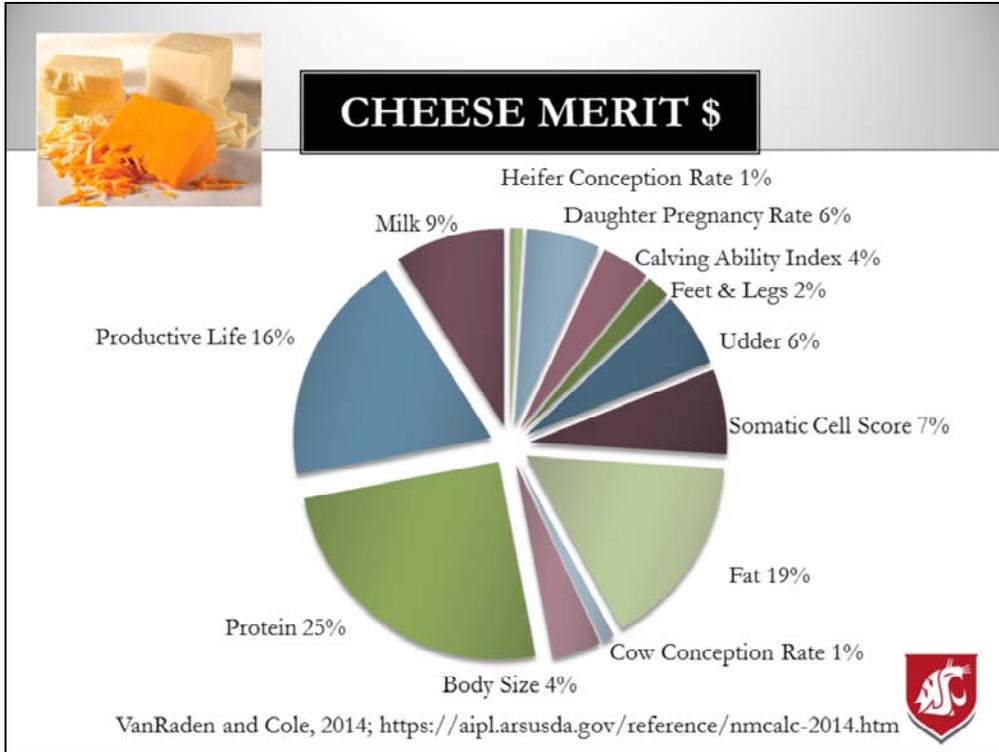
VanRaden and Cole, 2014; <https://aipl.arsusda.gov/reference/nmcalc-2014.htm>





Places more emphasis on milk production than either NM\$ or CM\$

Producers in Louisiana and Mississippi are paid for their milk based solely on skim and fat content of the milk. Therefore, FM\$ should be a more appropriate sire selection criterion in the SE milk market than either NM\$ or CM\$.



More emphasis on protein than NM\$, FM\$ or GM\$

## GRAZING MERIT DOLLARS



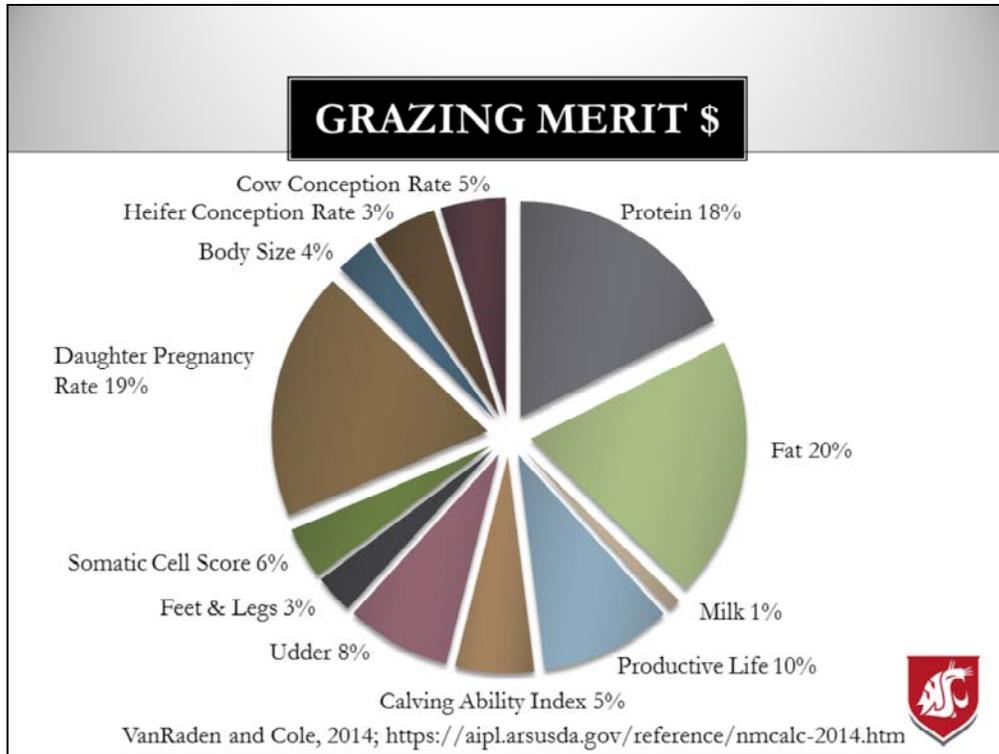
Introduced in 2014 for cows in grazing herds

Fertility is of high importance as most grazing herds participate on a seasonal breeding and calving system

- Management (health & fertility) comprises 46%
- Production comprises 39% with focus on pounds of fat and protein produced
- 15% comes from conformation

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More emphasis on Daughter Pregnancy Rate than NM\$, CM\$, FM\$

## TOTAL PERFORMANCE INDEX

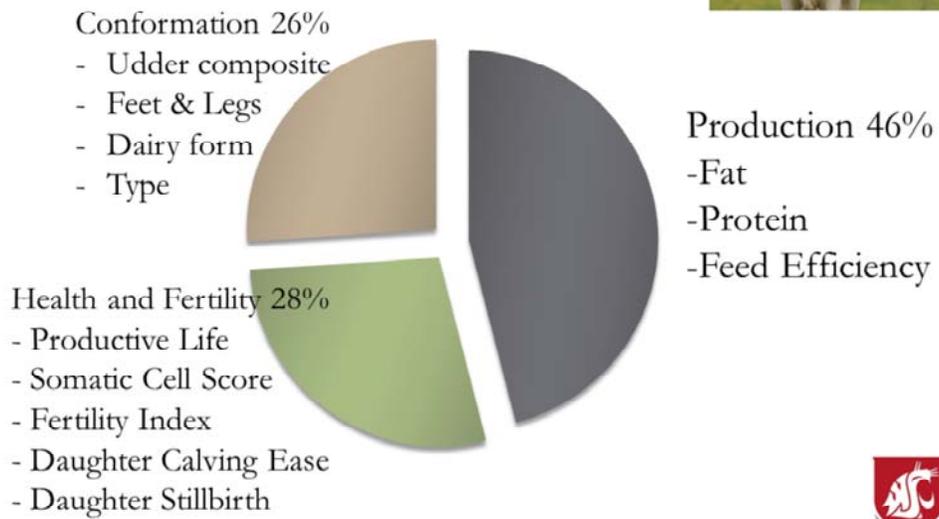
Selection index developed by the **US Holstein Association** as a representation of their vision for improvement of the domestic and international Holstein population

Traits are weighted rather than multiplied by an economic value (\$) as is done with NM\$

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## TPI (HOLSTEINS)



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## TPI

$$TPI = \left[ \begin{array}{l} \frac{27(PTAP)}{19.4} + \frac{16(PTAF)}{23.0} + \frac{3(FE)}{45} + \frac{8(PTAT)}{.73} - \frac{1(DF)}{1.0} + \frac{11(UDC)}{.8} + \frac{6(FLC)}{.85} \\ + \frac{7(PL)}{1.26} - \frac{5(SCS)}{.13} + \frac{13(FI)}{1.0} - \frac{2(DCE)}{1.0} - \frac{1(DSB)}{0.9} \end{array} \right] 3.8 + 2138$$

- |  |  |
|--|--|
| <ul style="list-style-type: none"> <li>• PTAP – protein</li> <li>• PTAF –fat</li> <li>• FE- feed efficiency</li> <li>• PTAT –type</li> <li>• DF – dairy form</li> <li>• UDC – udder composite</li> </ul> | <ul style="list-style-type: none"> <li>• FLC – feet &amp; legs composite</li> <li>• PTA – productive life</li> <li>• SCS – somatic cell score</li> <li>• FI – fertility index</li> <li>• DCE – daughter calving ease</li> <li>• DSB – daughter stillbirth</li> </ul> |
|--|--|



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2138 is an adjustment for base year

TPI is the selection index developed by the Holstein Association USA. The formula is comprised of 12 traits that are of economic significance for improving producer profitability and the Holstein breed. The udder composite index includes values on udder depth, fore udder attachment, rear udder height, rear udder width, udder cleft, front teat placement and rear teat placement. The feet and leg composite includes foot angle, rear legs from the rear and side view and a combined score. The body size composite index includes four measurements; stature, strength, body depth and rump width.

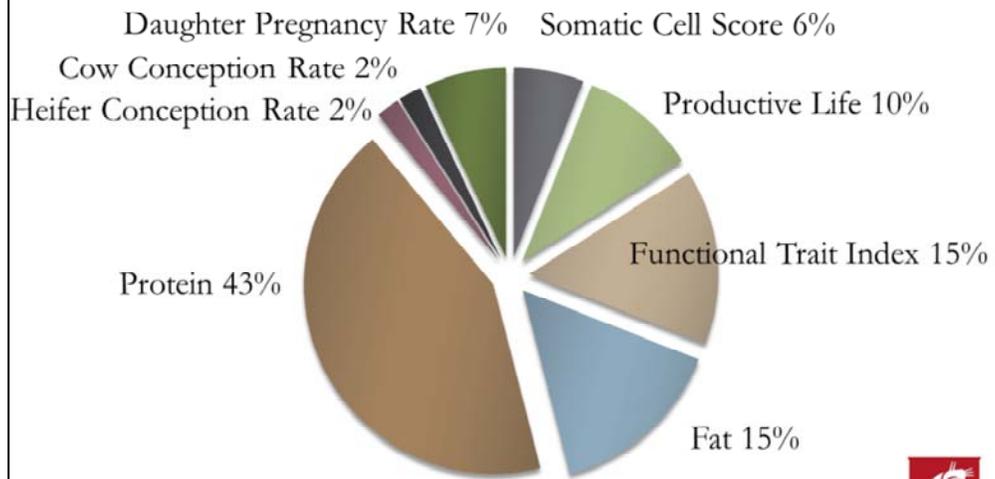
## JERSEY PERFORMANCE INDEX

- Selection index developed by the American Jersey Cattle Association with the over arching objective of increasing lifetime net income
- Developed from extensive evaluation of production, longevity, and health data to predict lifetime net profit from production, type, health, longevity and fertility traits



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## JERSEY PERFORMANCE INDEX



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## NEOGEN – IGENITY® TESTING

GGP HD150K \$92-96

- 150k SNPs
- Reliabilities of 71-74%
- Supports Holstein, Brown Swiss, Ayrshire



GGP LD \$42-46

- ≈42k SNPs
- Reliabilities of 68-72%
- Supports Holstein, Brown Swiss, Ayrshire, Jersey, Guernsey, Gyr, Girolando



Product comparisons:

[http://genomics.neogen.com/pdf/Igenity/AG258\\_IgenityCommercialDairyProductComparison.pdf](http://genomics.neogen.com/pdf/Igenity/AG258_IgenityCommercialDairyProductComparison.pdf)

GGP HD supports Holstein, brown Swiss, Ayrshire, reliabilities of 71-74%; \$92-96

GGP LD supports Holstein, Jersey, Brown Swiss, Ayrshire, Guernsey, Gyr, Girolando, reliabilities of \_\_\_\_\_; imputed to 66k?

Igenity prime 68-72, 42K \$42-46

The genotypes from these tests are sent to the USDA-CDCB where they are entered and compared with the USA herds for that breed. The Igenity Prime and Select are imputed up to 66k SNPs.

Select supports Holstein, Jersey, Brown Swiss; reliabilities of 67-71%

Essential - **15 key traits for sorting heifers as an alternative to USDA selection index for Jersey and Holstein cattle; reliabilities**

of 60-65%

Igenity-Basic returns a 1-10 score for ease of use rather than PTAs; crossbred product

## NEOGEN – IGENITY® TESTING

Igenity® Select \$37-40

Igenity-Select

- 45 traits goes to CDCB
- 9k with custom content SNPs
- Reliability 67-71%

Igenity® Essential \$29-32

Igenity-Essential

- 15 production traits, doesn't go to CDCB
- 9K with custom content SNPs
- Reliability 60-65%
- 15 key traits for sorting heifers



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Select supports Holstein, Jersey, Brown Swiss; reliabilities of 67-71%

Essential - **15 key traits for sorting heifers as an alternative to USDA selection index for Jersey and Holstein cattle; reliabilities of 60-65%**

Igenity-Basic returns a 1-10 score for ease of use rather

than PTAs; crossbred product

## EXAMPLE IGENITY® REPORT ON KEY TRAITS

ID	GM\$	NM\$	NM\$ Rank	NM\$ USA % Rank	Milk Yield	Fat lbs	Pro lbs	SCS	PL	DPR	DCE	IPI
1	635	627	1	99%	1102	49	30	2.84	5.8	2.7	5.8	2363
2	577	597	2	99%	1192	53	39	2.65	5.5	1.8	6.8	2322
3	360	375	4	98%	1431	26	28	2.95	3.4	0.9	5.9	2066

- **GM\$** - grazing merit \$
- **NM\$** - net merit \$
- **SCS** - somatic cell score
- **PL** – productive life
- **DPR** – daughter pregnancy rate
- **DCE** – daughter calving ease
- **Milk yield** – differences in pounds of milk for a 305 day lactation
- **Fat lbs** – differences in pounds of fat for a 305 day lactation
- **Pro lbs** – difference in lbs. of protein yielded for 305 day lactation
- **IPI** – Igenity production index (same as TPI)
- **SCE** - Sire calving ease
- **HCR** - Heifer conception rate
- **CCR** - Cow conception rate
- **DSB** - Daughter stillbirth
- **SSB** - Sire service stillbirth



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Sce, hcr, ccr, dsb,ssb

## IGENITY® DASHBOARD

- Interactive tool for interpreting genomic results
- Customize, sort, filter results
- Create custom indexes
- Designate a consultant where they can have access to data
- Compare rates of genetic gain between your and other herds
- <https://www.igenitydashboard.com/Home/Login>

**Igenity Dairy  
Dashboard**

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Scs, hcr, ccr, dsb,ssb, haploypc

## ZOETIS TESTING

Clarifide® \$39.50-42.50

- >20K SNPs
- Reliability 70-71%

Clarifide® \$79-86

- 62K SNPs
- Reliability 72-75%
- Jersey, Brown Swiss

Clarifide® Ultra Plus \$79-86

- Holstein
- Reliability 73%
- Includes Dairy Wellness Profit Index (DWP\$)
- Includes Wellness Trait Index (WT\$)



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Clarifide 17,500 markers reported to CDCB from >20K; delivers 70-71% reliability; \$39.50-42.50

Clarifide Ultra nearly 62,000 markers with 61K going to CDCB and 72-75% reliability; jersey and brown swiss \$79-86

Clarifide Ultra Plus designed specifically for wellness traits in US cattle and includes new Dairy Wellness Profit Index (DWP\$) based on traits that affect health, performance and profit in Holsteins with an average reliability of 50% for 6 wellness traits or Wellness Trait Index (WT\$) (includes markers for mastitis, lameness, metritis, retained placenta, displaced abomasum, ketosis)

Composite indexes Net Merit \$, Cheese Merit \$, Fluid Merit \$, Grazing Merit \$, Total Performance Index (TPI),

Reliability 73%

# CLARIFIED ULTRA PLUS



CDCB OFFICIAL EVALUATION	+	WELLNESS TRAITS	+	GENETIC CONDITIONS
PARENTAGE		MASTITIS		POLLED (NO FEE)
PRODUCTION		LAMENESS		
REPRODUCTION		METRITIS		MILK COMPONENTS
HEALTH		RETAINED PLACENTA		INFERTILITY HAPLOTYPES
TYPE		DISPLACED ABOMASUM		OTHER GENETIC CONDITIONS*
		KETOSIS		

\* CVM, Brachyzooina and Beta Casein A2 available with add-on fee.



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Wellness traits – research should be based on US Holsteins populations, have large numbers (had millions), see article in JDS, january 2017 and validation coming out soon; reliabilities about 50%; metritis 12% to 25%



# CLARIFIDE®

**5** Full Composite Indexes

Net Merit \$, Cheese Merit \$, Fluid Merit \$, Grazing Merit \$, Total Performance Index (TPI),

**5** Production Traits

Milk Volume, Fat Volume, Protein Volume, Fat %, Protein%

**4** Milk Protein Components

Alpha S-1 Casein, Beta Lactoglobulin, Kappa Casein I & II, Beta Casein A2\*

**11** Health & Repro Traits

SCS, DPR, HCR, CCR, Productive Life, Calving Ability, Sire & Daughter Calving Ease, Sire & Daughter Still Birth., Fertility Index Liveability

**MANY** Risk Mgmt Related

Specific Recessives: BLAD, DUMPS, Mulefoot, Chondrodysplasia, Citrullinemia, Factor XI, CVM\*, Brachyspina\*, 5 Breed Fertility Haplotypes

**22** Type Traits & Indexes

18 Linear Conformation Traits, Type-Final Score, and Udder, Feet & Leg, and Body Size Composites.

**5** Parentage & Inbreeding Info

Parentage (Sire & Dam), Maternal Grand Sire, Individual Genomic Inbreeding %, Future Inbreeding %.

**3** Additional Genetic Characteristics

Recessive Red (or Black), and Dominant Red coat color, Polled/Horned Gene\*

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Liveability released in august survive through lactation

## ZOETIS ENLIGHT

- Reporting and analysis of results
- Benchmarking
- Youngstock, whole herd and individual reports
- Access databases such as TPI and NM\$
- Interactive graphs



<https://www.zoetisus.com/animal-genetics/dairy/enlight.aspx>  
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## USING GENOMIC SELECTION

**Who** to genotype?

- Identify replacements, sell or send other heifers to feedlot
- Rank females for mating decisions



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## USING GENOMIC SELECTION

### When to genotype?

- First 30 days
- Post-weaning (6 months)



### Inform mating decisions

- Elite females – sexed semen, better bulls, ET donors
- Poorer females – beef bulls



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## CONCLUSIONS

- Genomic selection improves reliability, facilitates early selection, increases rate of genetic gain and performance at an unprecedented rate
- SNPs, as predictors of performance, need to be tested and validated in different breeds unless causative
- Many tools (selection indexes and genotyping assays) to use for multiple trait selection
- Timing and extent of genotyping depends on goals and level of investment

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