

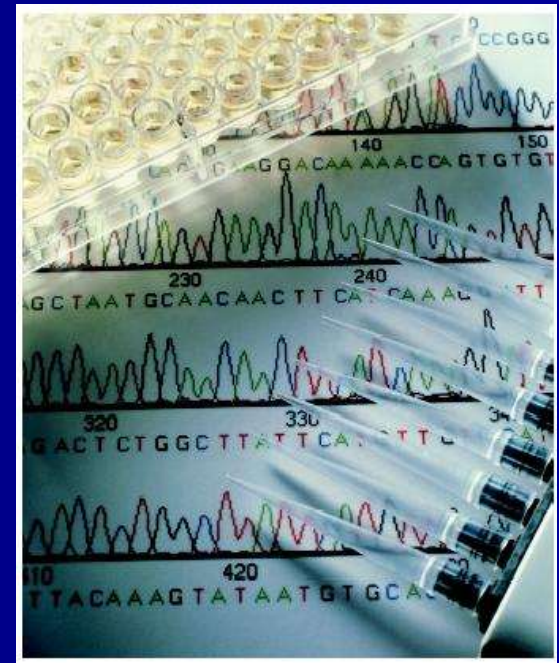
# Whole Genome-Assisted Selection



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<http://animalscience.ucdavis.edu/animalbiotech/>



# Overview

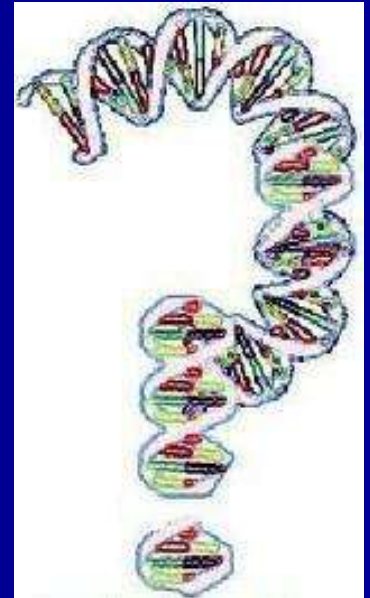
- Background
- Marker-assisted selection (MAS)
- What went wrong with MAS?
- Whole genome-assisted selection (WGS)
- Implications for breed associations





# Traditional Genetic Evaluation and EPD-based Selection

Selection on EPDs (derived from the observable performance of the animal and its relatives) has the effect on increasing the frequency of favorable alleles (and sometimes unfavorable alleles) without knowing the corresponding genes and molecular mechanisms





# Commercial companies are now offering DNA markers for use in Marker-Assisted Selection (MAS) for given traits



**Marker-assisted selection** is the process of using the results of DNA testing to assist in the selection of individuals to become parents in the next generation.





[Home](#)
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[News](#)
[Outreach](#)
[Marker Assisted Selection](#)

# Animal Biotechnology

Marker-Assisted Selection and Breeding

Alison L. Van Eenennaam

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[Cloning](#)
[Transgenics](#)
[Concerns](#)
[Marker-Assisted Selection and Breeding](#)



[DNA Markers: Explanation of Validation and Utilization \(2007\)](#)

Van Eenennaam, A. L. 2006. "DNA-Based Biotechnologies" Pages 66-73 in the National Beef Cattle Evaluation Consortium Beef Sire Selection Manual (2006)

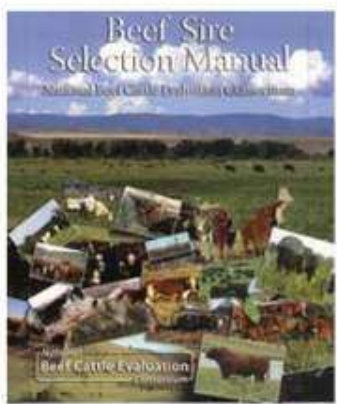
[Marker-Assisted Selection in Beef Cattle Handout \(4/07\)](#)

[Marker-Assisted Selection in Beef Cattle Slide Show](#)

[Marker-Assisted Selection DNA Backgrounder Handout](#)

[Peer-reviewed studies on current commercial DNA marker tests](#)

[National Beef Cattle Evaluation Consortium](#)



[NBCEC Beef Sire Selection Manual](#) - National Beef Cattle Evaluation Consortium (2006)

### Companies

#### Biogenetic Services

Cattle: Parentage, freemartin, coat color, leptin, meat quality, BSE resistance, Johne's disease  
 Sheep: Scrapie, Spider lamb syndrome  
 Fish: Whirling disease

#### Bovigen

Cattle: GeneSTAR® Quality Grade\*, GeneSTAR® Tenderness\*, GeneSTAR® BLACK, parentage, identity tracking

#### GeneSeek

Sheep: Scrapie  
 Cattle: Parentage, coat color Seek-Black Seek-

**Current listing of DNA companies maintained on "UC Davis Animal Biotechnology" website**

<http://animalscience.ucdavis.edu/animalbiotech>



# Tests for quantitative traits – currently 10-100 SNPs

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



# Tests for quantitative traits

**Bovigen**

**Igenity**

**MMI**

**Quality Grade**

**Tenderness**

**Other**

|                                  |  |   |
|----------------------------------|--|---|
| Results reported as No. of stars | Results reported on scale 1-10   | Results reported as "MGV"                           |
| GeneSTAR Quality Grade           | Igenity Profile – Quality Grade  | Tru-Marbling  |
| GeneSTAR Tenderness              | Igenity Profile - Tenderness   | Tru-Tenderness                                      |
| Feed Efficiency                  | Igenity Profile – Yield Grade, Fat thickness, Marbling, Hot carcass weight, Ribeye area. | Average daily gain (not commercially available yet) |

Validated by NBCEC



# http://www.nbcec.org/nbcec/

Address http://www.nbcec.org/nbcec/

*National* Colorado State University-Cornell University-University of Georgia

## Beef Cattle Evaluation

*Consortium*

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[Home Page](#)

[Home](#)   [Background](#)   [Sample Populations](#)   [Marker-Assisted Selection](#)   [Glossary](#)

### Commercial genetic test validations

[GeneSTAR<sup>®</sup> Tenderness](#)   [GeneSTAR<sup>®</sup> Quality Grade](#)   [iGENITY TenderGene™](#)   [Ancillary Results](#)



The purpose of the NBCEC commercial DNA test validation is to independently verify associations between genetic tests and traits as claimed by the commercial genotyping company using phenotypes and DNA from reference cattle populations.

The validation process is a partnership of the owners of DNA and phenotypes (e.g., breed associations) and genomics companies, facilitated by the NBCEC

[Home](#)

[Background](#)

[Sample Populations](#)

[Marker Assisted Selection](#)

[Glossary](#)

A. L. Van Eenennaam, J. Li, R. M. Thallman, R. L. Quaas, M. E. Dikeman, C. A. Gill, D. E. Franke, M. G. Thomas. 2007. Validation of commercial DNA tests for quantitative beef quality traits. *Journal of Animal Science*. 85:891-900.





# What went wrong with Marker-Assisted Selection (MAS) ?

- Currently available markers collectively account for 10% or less of the genetic variation
- 3-4 markers is not enough for quantitative traits
- Hard to find all genes that affect a single trait
- Markers do not exist for many important traits
- Early adopters of genotyping for MAS in livestock have not experienced sufficient value capture i.e. they are too expensive !

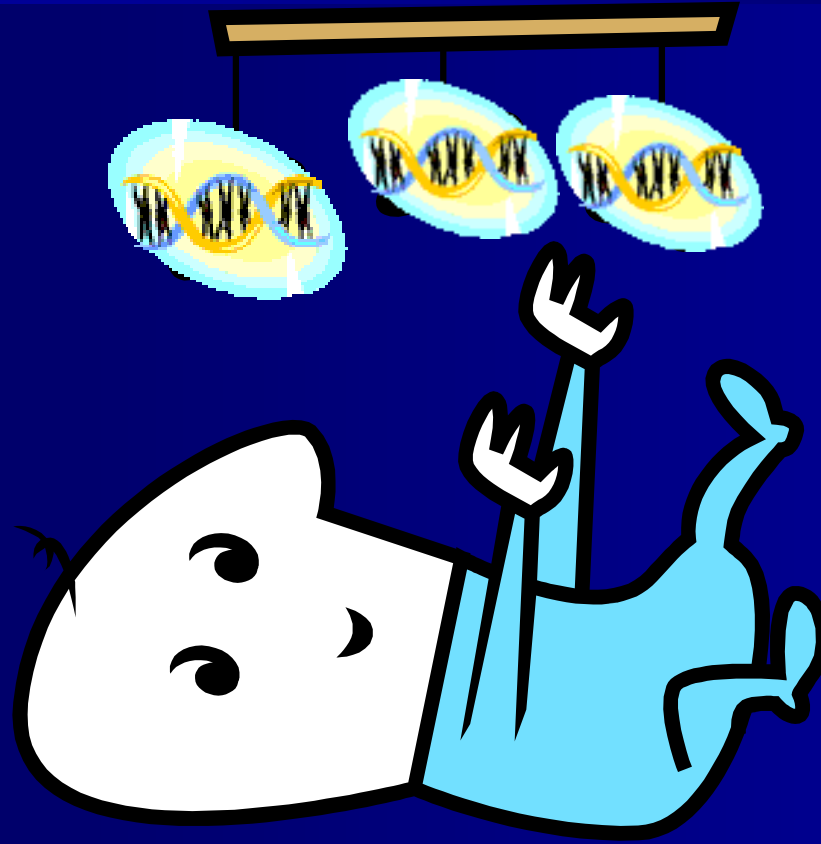


# And DNA data is not being used in national cattle evaluation

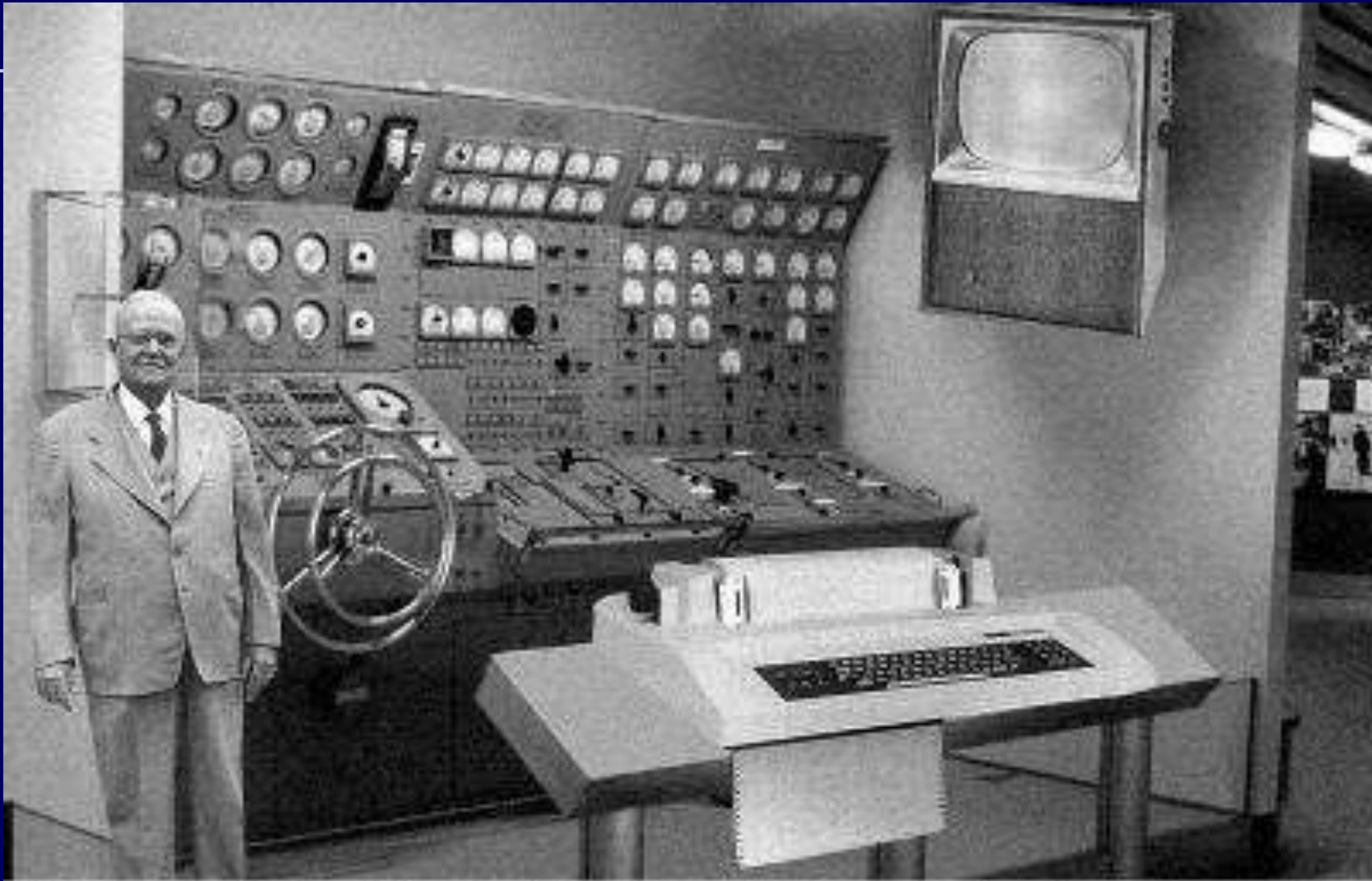
- Only a small proportion of the population is being genotyped
- Individual producers may be reluctant to share results for animals that are shown to have inherited unfavorable marker alleles.
- There is no national structure, at the breed association or any other level, to routinely capture genotypic information in a consistent form for the purpose of national evaluation.



# This is a young industry....



**“1954 version of what 'home computers' might look like in 50 years time (i.e. 2004)”**





# Wrong Expert Predictions

**“There is no reason anyone would want a computer in their home.”**

Ken Olson, president of Digital Equipment Corp. 1977

**“I think there's a world market for about five computers”**

Thomas J. Watson, chairman of the board of IBM. 1943



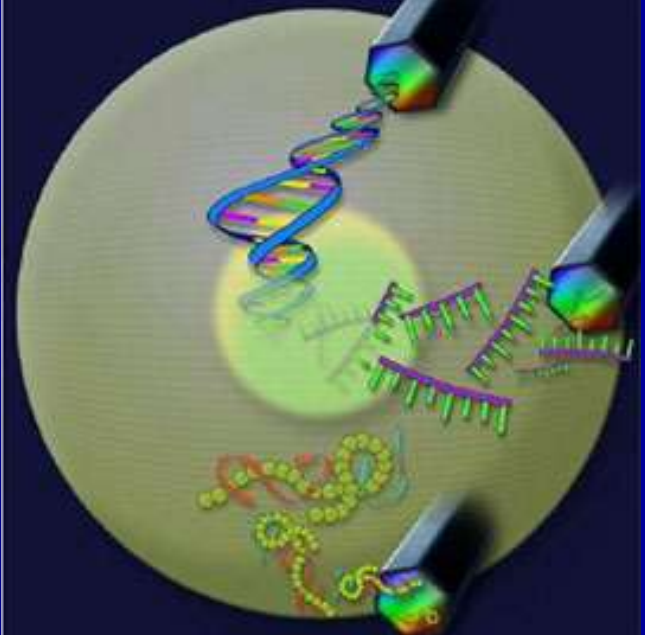
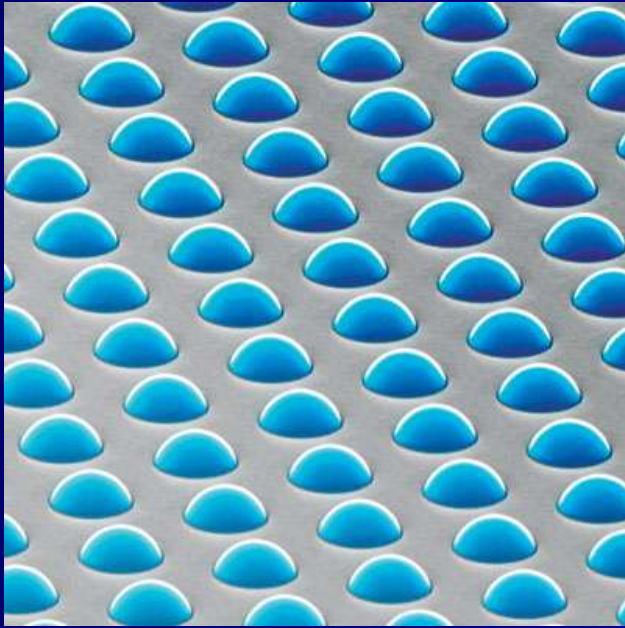
# High-throughput SNP genotyping on 50,000 SNP CHIP (50K Chip)



The sequencing of the bovine genome allowed for a collaboration between MARC, BARC, UMC and UA to develop a set of 50,000 SNPs that are located throughout the entire genome



# 12 samples per BeadChip can be run on 50,000 SNPs at ~ \$200/sample!





# Whole genome-assisted selection (WGS)

- The use of these dense markers across the entire genome enables an estimation of the genetic merit of every chromosome fragment contributing variation in a population with phenotypic observations
- Can simultaneously test 50,000 markers
- Can be used to predict merit for all traits for which phenotyped populations exist





# What is needed for whole genome-assisted selection?

## THEORY

- Population
- 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 predict the merit of new animals, not contained in the training data set



*WGS effectively estimates an EPD for every chromosome fragment in the genome*



# Possible applications

- Product quality
- Genetic disease resistance
  - Other difficult to phenotype traits
- Feed efficiency
- Health
- Robustness
- Adaptability
- Stayability
- Reproductive traits





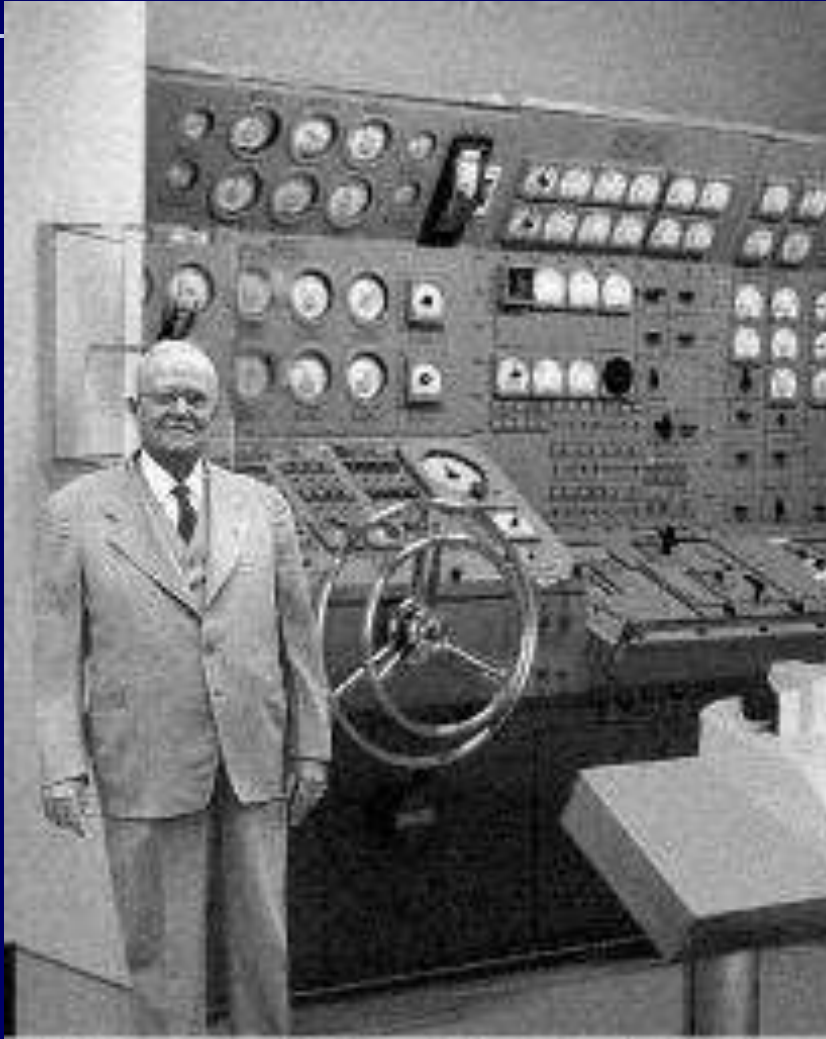
# WGS compared to MAS

Genomic selection uses the estimated effect of many loci at once, not just the small number of statistically significant loci that are a feature of MAS (Dorian Garrick, Iowa State University)

As there are so many variants detected in WGS, the properties of them as a group becomes more important than their individual effects...It matters little if a specific variant fails under some circumstances as long as the majority of the variants are predictive. (John McEwan, NZ)



**“what escaped their vision was that science might come up with new and different ways of commercializing and using new technologies.”**





# Marker-Assisted Selection (MAS)





# Whole Genome-enabled Selection (WGS)





***“There is no doubt that whole genome-enabled selection has the potential for being the most revolutionary technology since artificial insemination and performance-based index selection to change the nature of livestock improvement in the foreseeable future”***

Dorrian Garrick, Iowa State University





# Implications for Breed Associations

- Currently there are three competing SNP genotyping technologies – Affymetrix, Sequenom, and Illumina – prices are now less than 1 cent per SNP
- It is likely that SNP markers will replace alternatives (i.e. microsatellites) over the next 5 years



# SNPS and parentage

***"The low rate of genotyping errors meant that less than five inconsistencies were usually found when parent-progeny assignment was correct. However, several thousand inconsistencies were usually found when the parent-progeny assignment was incorrect"***

Wiggans et al. Genomic Evaluations in the United States and Canada: A collaboration. ICAR 2008



# Implications for Breed Associations

- Huge data processing, storage and analysis requirements.



# Developing genomic resources for whole genome selection.

J. C. McEwan. 2007.  
Proceedings of the New Zealand Society of Animal Production.67:148-153.

“DNA technology will be increasingly used on an industry wide basis. It increases information flow back to the breeder, thereby allowing better breeding decisions, provides parentage information, likely genetic worth of individuals, and provides an independent method to audit traceability. In the future **it will be the data processing, analysis, and electronic storage and transfer of results** that will be as much the challenge for increasing industry adoption rather than the DNA marker measurement technology.”



# Genomic Selection.

Goddard, M.E. and Hayes, B.J. 2007. *Journal of Animal Breeding and Genetics* 124:323-330.

- Unless all genomic EBV are calculated using the same prediction equation(s), they will no longer be comparable. A country is most likely to preserve a single EBV system if the database used to estimate the prediction equation is held by the national genetic evaluation system.
- However, this may inhibit commercialization of genomic selection because it makes it difficult for a company to recover the investment needed to develop and market a set of markers for genomic selection. The alternative would be for each company to have its own markers, database and EBV.



# Who/How will this technology be commercialized?

***"Keeping the characteristics of the fundamental evaluation system outside the realm of marketing will help the process remain unbiased and gain wider acceptance within the whole industry. "***

Wiggans et al. Genomic Evaluations in the United States and Canada: A collaboration.

ICAR 2008



# Genomic Selection.

Goddard, M.E. and Hayes, B.J. 2007. *Journal of Animal Breeding and Genetics* 124:323-330.

- Genomic selection separates the animals in the reference population, which is used to estimate the prediction equation, from the selection candidates. The animals in the reference population have phenotypes and genotypes, but the selection candidates need to have only marker genotypes.
- Except for the cost of genotyping, “stud” animals could be produced as cheaply as commercial animals. Then traditional stud breeders who record their animals with a breed association would be unable to compete with breeders who relied entirely on marker data.



# <http://animal.ifas.ufl.edu/extension/beef/shortcourse/2008/Garrick.pdf>

## "No Bull" Discussion on Genetic Markers

Dorian Garrick<sup>1</sup> and Alison Van Eenennaam<sup>2</sup>

<sup>1</sup>Professor, Iowa State University, Ames, IA

<sup>2</sup>Professor, University of California, Davis, CA

### Summary

Beef cattle production is a highly competitive activity and wise use of genetic resources and management options are required to ensure long-term profitability. Along with other food animal industries, genetic improvement provides one such opportunity for improved productive and economic efficiencies. Regardless of genetic merit, animal cohorts must be appropriately managed in order to maximize income over costs. Genetic markers provide promise for assisting with both these endeavors, namely increasing rates of genetic gain and providing new management opportunities. However, like all emerging technologies, they require considered use in order to provide economic benefits to the investor. This paper outlines some of the characteristics of these new and emerging genetic technologies.

### Alternative Opportunities for Genetic Markers

Livestock industries are typically characterized by several different production tiers that vary in many of their attributes including investment opportunities for the application of new technology. It is important for producers to recognize their own particular production circumstances when considering adopting new technology for the purpose of increased profitability. Broadly speaking, producers belong to either the seedstock (or bull selling) sector or the so-called commercial (or bull buying) sector. The

In the nucleus sector, the principal role for genetic markers is to increase the rate of genetic gain. The rate of genetic gain in the nucleus sector dictates the rate of genetic gain in the entire seedstock sector. The rate of genetic gain in the seedstock sector can be characterized for some traits by inspecting the graphs of genetic trends in EPDs that are published by Breed Associations in their sire catalogs and on their websites. These trends are incomplete for two reasons. First, they don't characterize all the economically-relevant traits. For example, fertility, longevity, and disease resistance traits tend to be under-represented in these catalogues. Second, they typically don't characterize the most important genetic change – that is the trend in overall profitability that would result from the simultaneous trends in the components of profit such as sale weights, calving ease, cow mature size, etc.

The annual rate of genetic change in the seedstock sector is dictated by three interacting components. These are the intensity of selection, the generation interval (or average age of parents when offspring are born), and the accuracy of selection. Annual advance from selection will be maximized when a few of only the very best candidates are selected and used widely at an early age. In practice, the accuracy of selection of young animals is limited for many of the economically-relevant traits, either because the traits have low heritability (e.g., reproductive traits), or they can only be measured late in life (e.g., longevity and carcass attributes) or under challenging conditions (e.g., disease or nutritional stress).

**Florida  
Extension  
Beef Cattle  
Short Course  
April 30 -  
May 2, 2008**





# California to host BIF 2009! Mark your calendars!

## 2009 Beef Improvement Federation Annual Research Symposium and Annual Meeting

### Sacramento, California April 30 – May 3, 2009



**CALIFORNIA**  
**BEEF RUSH '09**



Wednesday April 29<sup>th</sup>  
Thursday April 30<sup>th</sup>  
  
Friday May 1<sup>st</sup>  
Saturday May 2<sup>nd</sup>  
Sunday May 3<sup>rd</sup>

Early Registration  
Registration and Evening Reception  
Eastern Tour "Foothill Bovines, Equines and Fine Wines"  
Convention, Family/Spouse Tour, Evening Dinner  
Convention and Evening on your Own in Sacramento  
Western Tour "Ocean Wines and Bovines"



# Animal Biotechnology

## 30 minute-peer reviewed film

**Animal Biotechnology was developed to explain various forms of animal biotechnology, ranging from common applications such as artificial insemination, to the more controversial topics of genetic engineering and cloning. The movie is targeted to a general public audience.**

**Written and directed** by:  
Alison Van Eenennaam  
and Bill Pohlmeier

**Funding** provided by a  
USDA NRI grant





Questions ?

