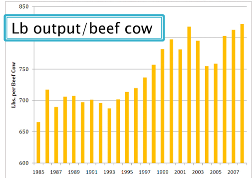
Genomics for the rancher: How does it work and what does it mean?

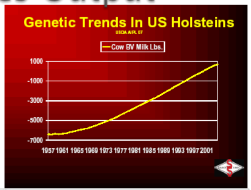
Dr. Jack Whittier
Extension Beef Specialist, Colorado State University
XXII Range Beef Cow Symposium, Mitchell, Nebraska
November 29, 30 and December 1, 2011

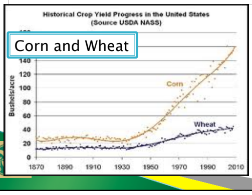
My Charge:

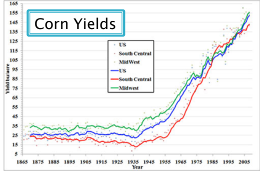
- Genomics – the basics
  - What it means
  - Is it something producers should be aware of and should be using?
  - If so, how should they use it to improve their herd and profitability?
    - I'll leave this to the next speaker, Matt Spangler

Selection Improves Output


Lb output/beef cow


Genetic Trends In US Holsteins
USDA AIPL 07

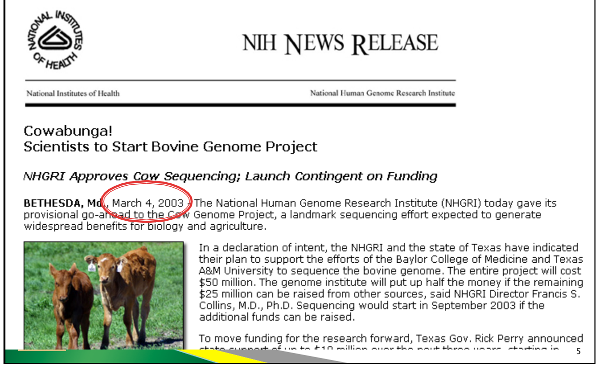

Corn and Wheat
Historical Crop Yield Progress in the United States
(Source USDA NASS)


Corn Yields

Questions:

- What are Marker-Enhanced (Marker-Assisted) EPDs? (MBV – Molecular Breeding Values)
- What can be learned from genomics?
- What tools are and have been used for genetic selection?
- What does genetic selection with genomic information have to offer?
- Should I be using Marker-Enhanced EPDs (MBVs) ?

Bovine Genome Sequence


NIH NEWS RELEASE

National Institutes of Health — National Human Genome Research Institute

Cowabunga!
Scientists to Start Bovine Genome Project

NHGRI Approves Cow Sequencing; Launch Contingent on Funding

BETHESDA, Md., March 4, 2003 - The National Human Genome Research Institute (NHGRI) today gave its provisional go-ahead to the Cow Genome Project, a landmark sequencing effort expected to generate widespread benefits for biology and agriculture.

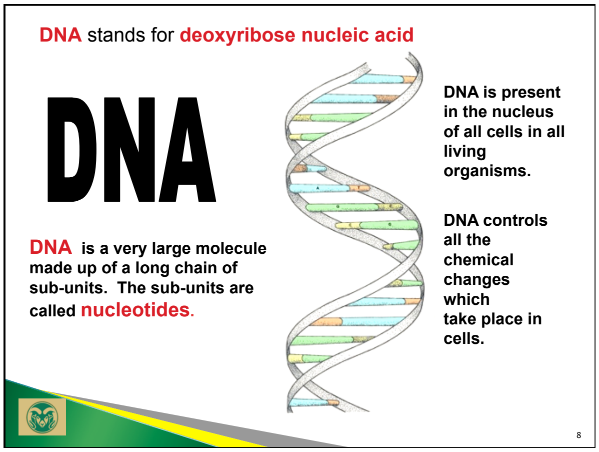
In a declaration of intent, the NHGRI and the state of Texas have indicated their plan to support the efforts of the Baylor College of Medicine and Texas A&M University to sequence the bovine genome. The entire project will cost $50 million. The genome institute will put up half the money if the remaining $25 million can be raised from other sources, said NHGRI Director Francis S. Collins, M.D., Ph.D. Sequencing would start in September 2003 if the additional funds can be raised.

To move funding for the research forward, Texas Gov. Rick Perry announced

The first cow genome to be sequenced was that of a Hereford cow named L1 Dominette, shown here with her calf. LARRS, Miles City, MT

Terminology

- Genome and Genomic
- DNA – Deoxyribonucleic acid
- Chromosomes
- Allele
- Genes
- Loci
- QTL – Quantitative Trait Loci
- Gene Markers
- SNPs – Single Nucleotide Polymorphism
- SNP Chips

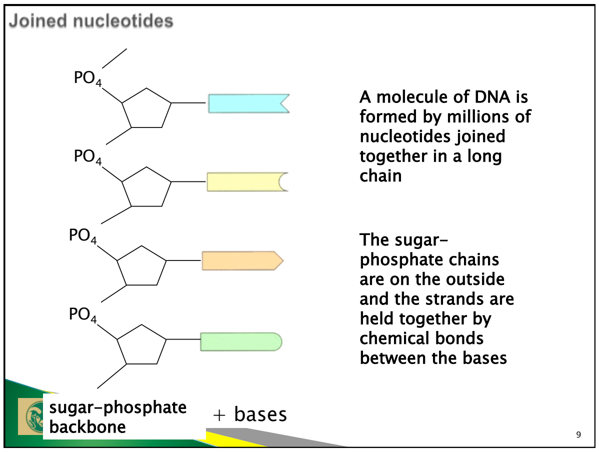


DNA stands for **deoxyribose nucleic acid**

DNA is a very large molecule made up of a long chain of sub-units. The sub-units are called nucleotides.

DNA is present in the nucleus of all cells in all living organisms.

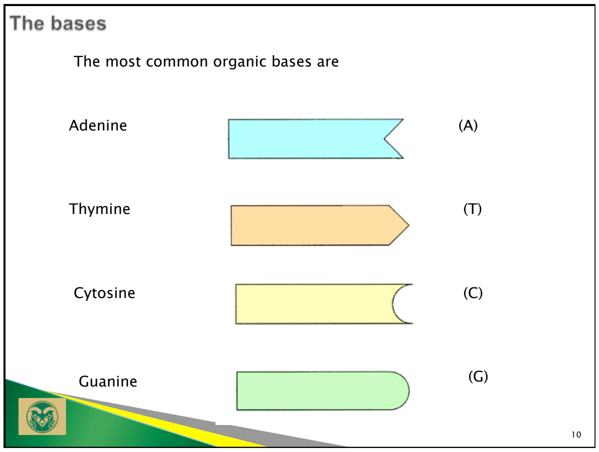
DNA controls all the chemical changes which take place in cells.



Joined nucleotides

A molecule of DNA is formed by millions of nucleotides joined together in a long chain

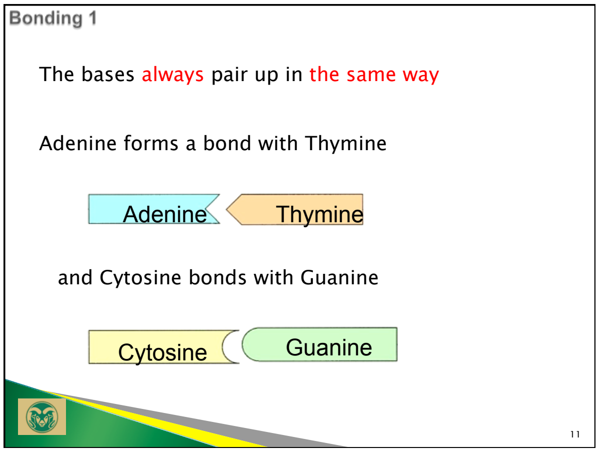
The sugar–phosphate chains are on the outside and the strands are held together by chemical bonds between the bases



The bases

The most common organic bases are

Adenine	(A)
Thymine	(T)
Cytosine	(C)
Guanine	(G)

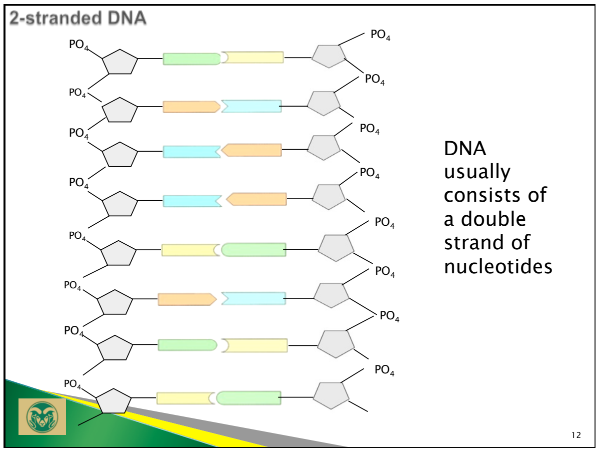


Bonding 1

The bases always pair up in the same way

Adenine forms a bond with Thymine

and Cytosine bonds with Guanine



2-stranded DNA

DNA usually consists of a double strand of nucleotides

Genetic code 1

The sequence of bases in DNA forms the Genetic Code

A group of three bases (a triplet) controls the production of a particular amino acid in the cytoplasm of the cell

The different amino acids and the order in which they are joined up determines the protein being produced

Genes

A sequence of triplets in the DNA molecule may code for a complete protein

Such a sequence forms a gene

There may be a thousand or more bases in one gene

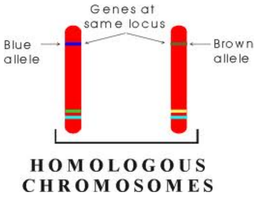
Chromosome

Cattle have 30 Chromosomes

An organized structure of DNA and protein that is found in cells. It is a single piece of coiled DNA containing many genes.

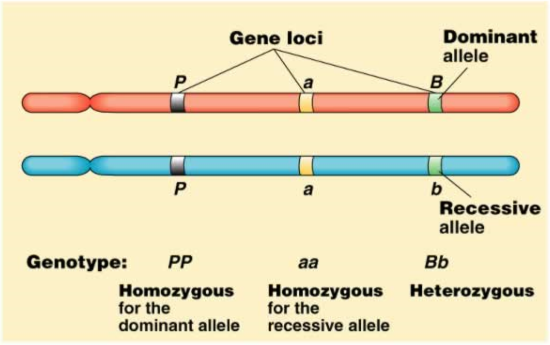
Allele

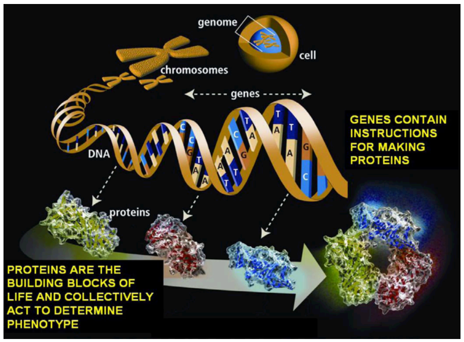
One member of a pair or series of genes that occupy a specific position on a specific chromosome.



Loci

The specific place on a chromosome where a gene is located.

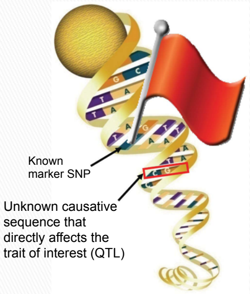




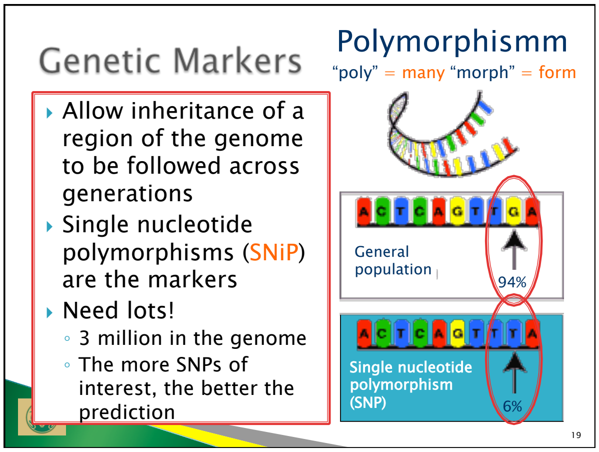
NBCEC Sire Selection Manual. Chapter 13 Figure 1. DNA (deoxyribonucleic acid) contains the instructions for making proteins. Differences in the nucleotide sequence of a gene's DNA can influence the type or amount of protein that is made, and this can have an effect on the observed performance of an animal. *Original graphic obtained from the U.S. Department of Energy Human Genome Program, http://www.doegenomes.org.*

Genetic Markers and Causative Loci

- A genetic marker **"single nucleotide polymorhism"** (SNP) flags the approximate location of DNA sequences having a direct effect on the trait.



Source: NBCEC Sire Selection Manual. Chapter 13. Figure 4.

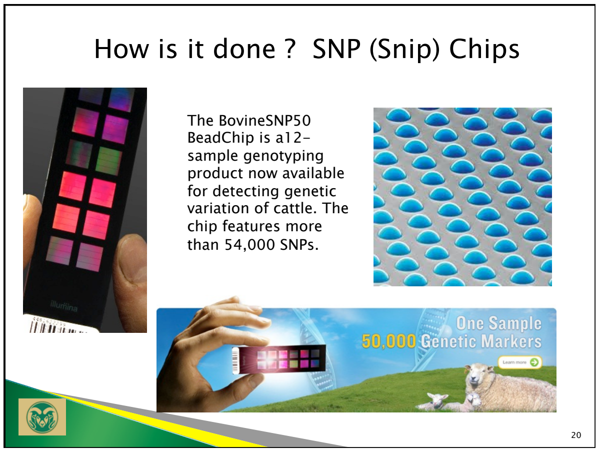


Genetic Markers

- Allow inheritance of a region of the genome to be followed across generations
- Single nucleotide polymorphisms (SNiP) are the markers
- Need lots!
  - 3 million in the genome
  - The more SNPs of interest, the better the prediction

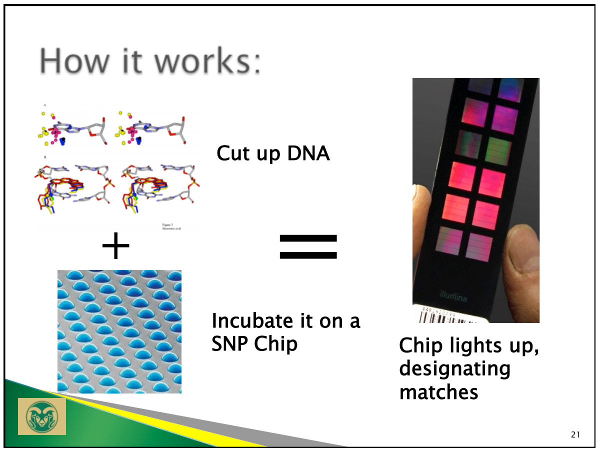
Polymorphismm

"poly" = many "morph" = form



How is it done ? SNP (Snip) Chips

The BovineSNP50 BeadChip is a12-sample genotyping product now available for detecting genetic variation of cattle. The chip features more than 54,000 SNPs.



How it works:

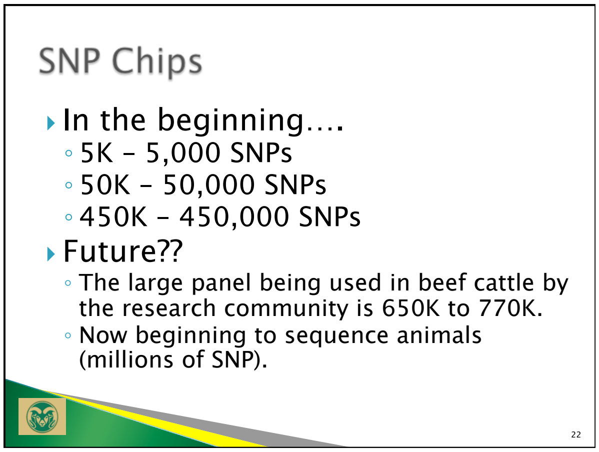
Cut up DNA

+

=

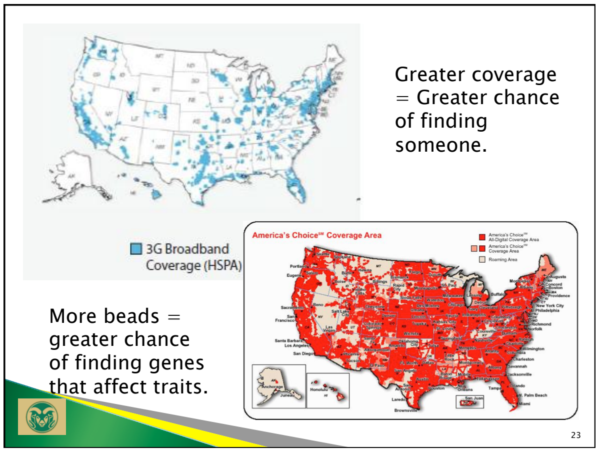
Incubate it on a SNP Chip

Chip lights up, designating matches



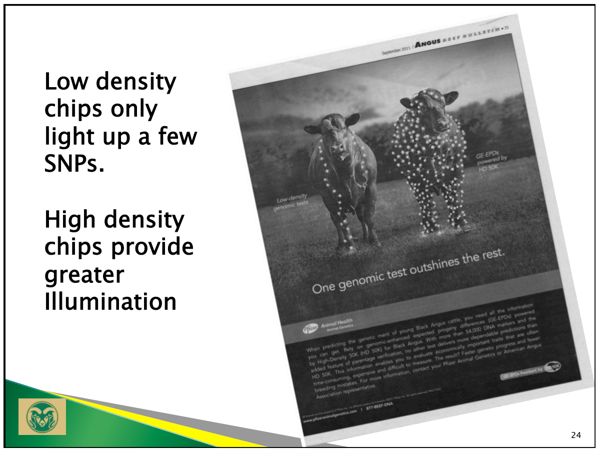
SNP Chips

- In the beginning….
  - 5K – 5,000 SNPs
  - 50K – 50,000 SNPs
  - 450K – 450,000 SNPs
- Future??
  - The large panel being used in beef cattle by the research community is 650K to 770K.
  - Now beginning to sequence animals (millions of SNP).



Greater coverage = Greater chance of finding someone.

More beads = greater chance of finding genes that affect traits.



Low density chips only light up a few SNPs.

High density chips provide greater Illumination

When predicting the genetic merit of young Black Angus cattle, you need all the information you can get. Rely on genomic-enhanced expected progeny differences (GE-EPDs) powered by High-Density 50K (HD 50K) for Black Angus. With more than 54,000 DNA markers and the added feature of parentage verification, no other test delivers more dependable predictions than HD 50K. This information enables you to evaluate economically important traits that are often time-consuming, expensive and difficult to measure. The result? Faster genetic progress and fewer breeding mistakes. For more information, contact your Pfizer Animal Genetics or American Angus Association representative.

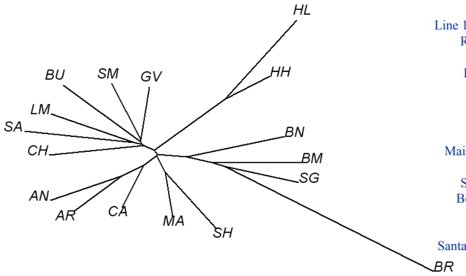
www.pfizeranimalgenetics.com | 877-BEEF-DNA

Example 1: Genetic Test for Genetic Defects

- Arthrogryposis Multiplex (AM)
  - Commonly called “curly calf syndrome”
  - Caused by a small mutation – 23,000 base deletion affecting 3 genes
- Test for mutation was developed in about 4 months by Dr. Beever at University of Illinois
  - Historical DNA was available
  - The bovine sequence was available
  - For a single gene, it took 80 animals

Source: Enns, Colorado Farm Show, 2011

Example 2: Genetic Distance Between Breeds as Estimated by the Correlations Among Frequencies for Markers on the Illumina Bovine SNP50



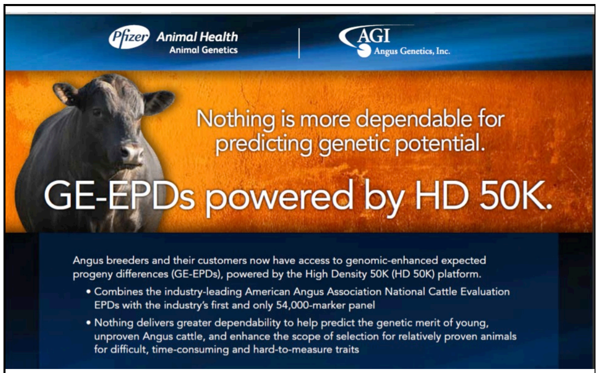
Angus (AN)
Hereford (HH)
Line 1 Hereford (HL)
Red Angus (RA)
Shorthorn (SH)
Braunvieh (BU)
Chianina (CA)
Charolais(CH)
Gelbvieh (GV)
Limousin (LM)
Maine-Anjou (MA)
Salers (SA)
Simmental (SM)
Beefmaster (BM)
Brahman (BR)
Brangus (BN)
Santa Gertrudis (SG)

L. A. Kuehn, et al. 2011. Predicting breed composition using breed frequencies of 50,000 markers from the U.S. Meat Animal Research Center 2,000 bull project.
J Anim Sci published online Jan 28, 2011

Example 3: Carcass Traits

Group	Quality Grade	GeneSTAR® Marbling Result		
		0	★	★★
Yearling-Fed	% Choice	58	62	74
	% Select	42	38	26
Calf-Fed	% Choice	34	41	53
	% Select	66	59	47
Yearling-Fed	Premium Choice	10	16	21

Source: Enns, Colorado Farm Show, 2011



Angus breeders and their customers now have access to genomic-enhanced expected progeny differences (GE-EPDs), powered by the High Density 50K (HD 50K) platform.

- Combines the industry-leading American Angus Association National Cattle Evaluation EPDs with the industry’s first and only 54,000-marker panel
- Nothing delivers greater dependability to help predict the genetic merit of young, unproven Angus cattle, and enhance the scope of selection for relatively proven animals for difficult, time-consuming and hard-to-measure traits

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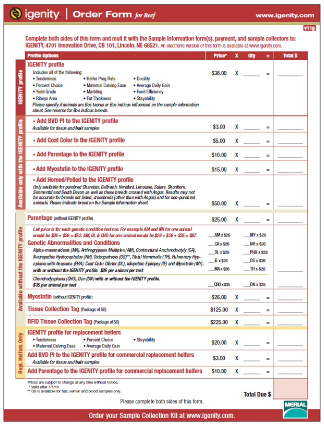
What tests?

What is the cost?



Complete both sides of this form and mail it with the Sample Information form(s), payment, and sample collectors to: IGENITY, 4701 Innovation Drive, CB 101, Lincoln, NE 68521. An electronic version of this form is available at www.igenity.com.

	Profile Options	Price*	X	Qty	=	Total $
IGENITY profile	IGENITY profile Includes all of the following: • Tenderness • Heifer Preg Rate • Docility • Percent Choice • Maternal Calving Ease • Average Daily Gain • Yield Grade • Marbling • Feed Efficiency • Ribeye Area • Fat Thickness • Stayability *Please specify if animals are Bos taurus or Bos indicus influenced on the sample information sheet. See reverse for Bos indicus breeds.*	$38.00	X	______	=	________
Available only with the IGENITY profile	• Add BVD PI to the IGENITY profile *Available for tissue and hair samples*	$3.00	X	______	=	________
	• Add Coat Color to the IGENITY profile	$5.00	X	______	=	________
	• Add Parentage to the IGENITY profile	$10.00	X	______	=	________
	• Add Myostatin to the IGENITY profile	$15.00	X	______	=	________
	• Add Horned/Polled to the IGENITY profile *Only available for purebred Charolais, Gelbvieh, Hereford, Limousin, Salers, Shorthorn, Simmental and South Devon as well as these breeds crossed with Angus. Results may not be accurate for breeds not listed, crossbreds (other than with Angus) and for non-purebred animals. Please indicate breed on the Sample Information sheet.*	$50.00	X	______	=	________
Available without the IGENITY profile	Parentage (without IGENITY profile)	$25.00	X	______	=	________
	List price is for each genetic condition test run. For example AM and NH for one animal would be $26 + $26 = $52. AM, DL & CHO for one animal would be $26 + $26 + $35 = $87. Genetic Abnormalities and Conditions *Alpha-mannosidosis (MA), Arthrogryposis Multiplex (AM), Contractural Arachnodactyly (CA), Neuropathic Hydrocephalus (NH), Osteopetrosis (OS)**, Tibial Hemimelia (TH), Pulmonary Hypoplasia with Anasarca (PHA), Coat Color Dilutor (DL), Idiopathic Epilepsy (IE) and Myostatin (MY), with or without the IGENITY profile. $26 per animal per test*	___AM x $26 ___CA x $26 ___DL x $26 ___IE x $26 ___MA x $26		___MY x $26 ___NH x $26 ___PHA x $26 ___OS x $26 ___TH x $26		________
	Chondrodysplasia (CHO), Dun (DN) with or without the IGENITY profile. $35 per animal per test	___CHO x $35		___DN x $35		________
	Myostatin (without IGENITY profile)	$26.00	X	______	=	________
	Tissue Collection Tag (Package of 50)	$125.00	X	______	=	________
	RFID Tissue Collection Tag (Package of 50)	$225.00	X	______	=	________
Repl. Heifers Only	IGENITY profile for replacement heifers • Tenderness • Percent Choice • Stayability • Maternal Calving Ease • Average Daily Gain	$20.00	X	______	=	________
	Add BVD PI to the IGENITY profile for commercial replacement heifers *Available for tissue and hair samples*	$3.00	X	______	=	________
	Add Parentage to the IGENITY profile for commercial replacement heifers	$10.00	X	______	=	________

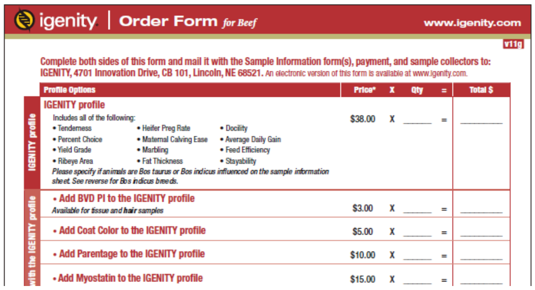
Prices are subject to change at any time without notice.
* Valid after 7/1/10
** OS is available for hair, semen and blood samples only.

Total Due $

Please complete both sides of this form.

Order your Sample Collection Kit at www.igenity.com.

MERIAL


igenity | Order Form for Beef
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Complete both sides of this form and mail it with the Sample Information form(s), payment, and sample collectors to: IGENITY, 4701 Innovation Drive, CB 101, Lincoln, NE 68521. An electronic version of this form is available at www.igenity.com.

	Profile Options	Price*	X	Qty	=	Total $
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with the IGENITY profile	• Add BVD PI to the IGENITY profile *Available for tissue and hair samples*	$3.00	X	______	=	________
	• Add Coat Color to the IGENITY profile	$5.00	X	______	=	________
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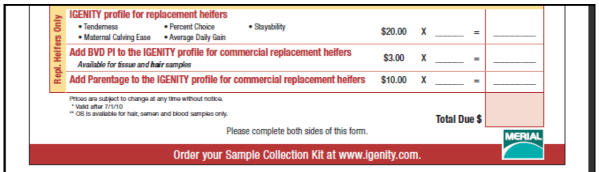

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Add Parentage to the IGENITY profile for commercial replacement heifers	$10.00	X	______	=	________

Prices are subject to change at any time without notice.
* Valid after 7/1/10
** OS is available for hair, semen and blood samples only.

Total Due $

Please complete both sides of this form.

Order your Sample Collection Kit at www.igenity.com.

- American Angus Association
  - GeneMax™
  - Commercial herds targeted
  - $15-20 per head

Traditional Selection Programs

EPDs

- Estimate genetic merit for animals in a population
- Select superior animals as parents of future generations
- Traditional selection has been very effective for many economically important traits

Genetic Evaluations – Limitations

- Slow!
  - Progeny testing for production traits take 3 to 4 years from insemination
  - A bull will be **at least 5 years old** before his first evaluation is available
- Expensive!
  - Progeny testing costs $25,000 per bull
  - Only 1 in 8 to 10 bulls graduate from progeny test
  - At least $200,000 invested in each active bull!!

Advantages of MAS

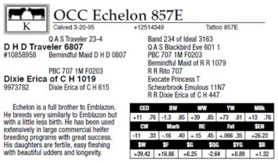
- **Simpler method compared to phenotypic screening**
  - Especially for traits with expensive screening
  - May save time and resources
- **Selection at earlier (birth?) stage**
  - Important for traits such as defects, polledness, birth weight, growth, you name it
  - Can screen before investing in progeny testing
- **Increased reliability (accuracy)**
  - Minimized environmental effects

SNP Derived Molecular Breeding Values (MBV)

- What is the relationship between phenotype and this genomic technology?
- The process:
  - "Train" the computations on animals with known performance and SNP data
  - Use these relationships to calculate MBVs on other individuals
- A weakness:
  - These relationships amongst SNPs of one breed are not the same in other breeds
  - What about cross-bred animals?

Source: Enns, Colorado Farm Show, 2011

When considering bull decisions............



K

OCC Echelon 857E
Calved 3-20-95 +12514349 Tattoo 857E

Q A S Traveler 23-4
D H D Traveler 6807
#10858958 Bemindful Maid D H D 0807

PBC 707 1M F0203
Dixie Erica of C H 1019
9973782 Dixie Erica of C H 615

Band 234 of Ideal 3163
Q A S Blackbird Eve 601 1
PBC 707 1M F0203
Bemindful Maid of R R 1079
R R Rito 707
Evocate Princess T
Schearbrook Emulous 11N7
R R Dixie Erica of C H 447

Echelon is a full brother to Emblazon. He breeds very similarly to Emblazon but with a little less birth. He has been used extensively in large commercial heifer breeding programs with great success. His daughters are fertile, easy fleshing with beautiful udders and longevity.

CED	BW	WW	YW	Milk
+11 .76	-1.3 .85	+39 .85	+73 .81	+13 .76
CW	**Marb**	**RE**	**Fat**	**$EN**
-11 .33	-.16 .40	+.15 .45	+.006 .35	+26.23

$W	$F	$G	$QG	$YG	$B
+39.42	+16.86	+6.25	-2.64	+8.89	+1.32

Full brother to Emlazon

- How do they look?
- What is their pedigree?
- How did they perform?
- How did their progeny perform?
- What is the dollar value of their genetic performance (index)?
- **What is their genetic code and how can I use it to improve my decisions?**

An Analogy from Baseball and Conclusion

Moneyball – The movie

Peter Brand (Jonah Hill)
The Statistician

Billy Beane (Brad Pitt)
Oakland A's GM 2002

Moneyball – Starring Brad Pitt

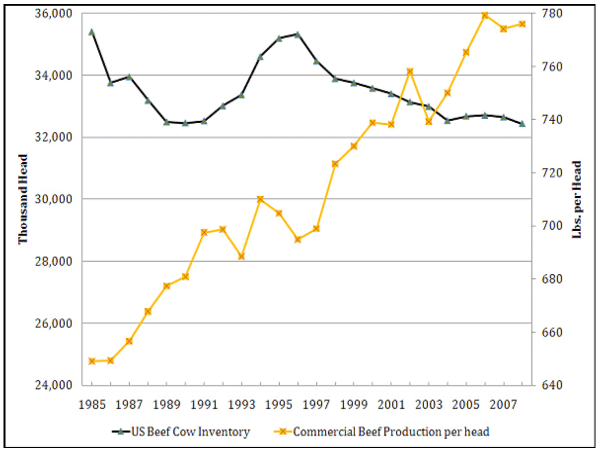
- The central premise of *Moneyball* is that the collected wisdom of baseball insiders (including players, managers, coaches, scouts, and the front office) over the past century is subjective and often flawed.
- Player statistics such as stolen bases, runs batted in, and batting average, typically used to gauge players, are leftovers of a 19th century view of the game and the player information that was available at the time.
- The movie argues that the Oakland A's' front office took advantage of more empirical gauges of player performance to compete successfully against richer competitors in Major League Baseball.

The lesson…

- Rigorous statistical analysis demonstrated that on-base percentage and slugging percentage are better indicators of offensive success that the traditional player statistics used to select players by other teams

The analogy….

- So, with the development of genomics, predictors like molecular breeding values (MBVs) for Economically Relevant Traits (ERTs) may allow cattle producers better ways to identify valuable animals using "outcome statistics" coupled with DNA markers – much like the Oakland A's were able to find undervalued players by using actual performance outcome like on-base percentages.
- New tools such as genomics provide a new method to gain enhanced genetic information without the time and expense required to test a large number of progeny.



Summary and Conclusion

- Markers are not a replacement of EPDs
- Good genetics will never overcome poor management (environment)
- MAS is likely to accelerate genetic progress in some traits better than others
- Ensure you weigh the cost and benefits of using MAS in your production system just as you would with any other input

Thank You! Questions?