

ANIMAL GENOMICS @ MIZZOU **It's Been An Important Week In Cattle Genomics**
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Genome-Wide Survey of SNP Variation Uncovers the Genetic Structure of Cattle Breeds
 The genetic structure and gene flow in the genome of cattle have been investigated using a genome-wide survey of single nucleotide polymorphisms (SNPs). The study reveals the genetic relationships between different cattle breeds and provides insights into the evolution of the species.

The Genome Sequence of Taurine Cattle: A Window to Ruminant Biology and Evolution
 The complete genome sequence of taurine cattle has been determined, providing a valuable resource for studying ruminant biology and evolution. The sequence reveals numerous genes and regulatory elements that are unique to ruminants and offers insights into their specialized digestive systems and other biological features.

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ANIMAL GENOMICS @ MIZZOU What Are SNPs?

• SNP stands for **Single Nucleotide Polymorphism**

• SNPs are DNA variants that occur as single base changes

a SNPs

SNP SNP SNP

Chromosome 1 A A C A G C C C A T T C G G G G T C A G T C G A C C G
 Chromosome 2 A A C A G C C C A T T C G G G G T C A G T C A A C C G
 Chromosome 3 A A C A T G C C A T T C G G G G T C A G T C A A C C G
 Chromosome 4 A A C A G C C C A T T C G G G G T C A G T C A A C C G

b Haplotypes

Haplotype 1 C T C A A A G T A C G G T T C A G G C A
 Haplotype 2 T T C A T T T C G C C A A C A G T A A T A
 Haplotype 3 C C G A T C T G T A T A C T G T G T G
 Haplotype 4 T T C A T T C G C G G T T C A G A C A

c Tag SNPs

A T C
 G C G

ANIMAL GENOMICS @ MIZZOU What's Cool About SNPs?

We find SNPs by sequencing the DNA of many animals

• 62,000 cow SNPs
 • 375,000 pig SNPs
 • 5 million cow SNPs???

From 50,000 to 1 Million SNPs can be simultaneously assayed on a SNP Chip

• 58,383 cow SNPs
 • 64,232 pig SNPs

nature methods

ANIMAL GENOMICS @ MIZZOU **How Do We Currently Estimate EBVs?**

$$\begin{bmatrix} X'X & X'Z \\ Z'X & Z'Z + A^{-1}\alpha \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'Y \\ Z'Y \end{bmatrix}$$

Pedigree Relationships
Heritability
Breeding Values
Data

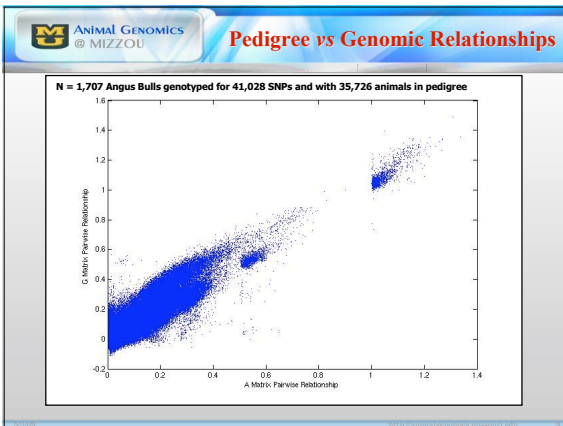
- Breeding values are the sum of the effects of all genes (2 copies per gene) in the genome that cause variation in trait
- You must have accurate pedigrees and lots of data available early in animals' lives...
 - That's why we don't have EPDs for Feed Intake...

ANIMAL GENOMICS @ MIZZOU **Pedigree vs Genomic Relationships**

Bull A Genome

Bull B Genome

- Pedigree relationships reflect the average number of genes shared identical by descent (IBD) between two individuals
- We can estimate the actual number of genes IBD using SNP genotype data



ANIMAL GENOMICS @ MIZZOU **EPDs via Genomic Relationships**

$$\begin{bmatrix} X'X & X'Z \\ Z'X & Z'Z + G^{-1}\lambda \end{bmatrix} \begin{bmatrix} \hat{b} \\ \hat{u} \end{bmatrix} = \begin{bmatrix} X'Y \\ Z'Y \end{bmatrix}$$

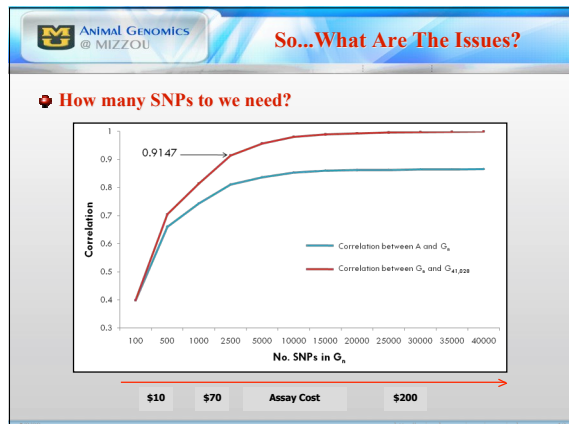
- We can compute EPDs using the actual identity by descent between individuals
 - We don't need pedigrees!
 - We don't need all animals to have data!
 - The heritability usually increases substantially!
- The produced EPDs are Molecular EPDs or Genome-Assisted EPDs and their implementation facilitates Genomic Selection

ANIMAL GENOMICS @ MIZZOU **An Example...**

$$\begin{bmatrix} X'X & X'Z & 0 \\ Z'X & Z'Z + G^{ss} & G^{sb} \\ 0 & G^{bs} & G^{bb} \end{bmatrix} \begin{bmatrix} \hat{pen} \\ \hat{u}_s \\ \hat{u}_b \end{bmatrix} = \begin{bmatrix} X'Y_s \\ Z'Y_s \\ 0 \end{bmatrix}$$

698 Angus steers with 85 Sires + ~600 Dams + individual Feed Intake (AFI) 1,707 Angus bulls

1,707 AFI EBVs
 Acc. = 0.15-0.64
 Av. Acc. = 0.27



ANIMAL GENOMICS @ MIZZOU **So...What Are The Issues?**

- **The 50K test reagents cost ~\$200**
 - How many of you are willing to pay \$200-\$400 for a test?
 - Even if that test gives you EPDs for growth, carcass, heifer pregnancy, feed efficiency, palatability and shear force?
- **The dairy experience is that you need to genotype ~6,000 bulls with PTAs to get Accuracies to ~70%**
 - 20K SNPs work as well as 40K SNPs...see last slide...
 - Where do I go to get DNA on 6,000 Angus bulls?
- **A test developed in Angus may not work in other breeds**
 - We are testing this in 2,200 genotyped Limousin
- **Can we get >70% Accuracies and across breed tests?**
 - We will need >6,000 animals with DNA and EPDs or phenotypes
 - We will need a 1Million SNP chip and it needs to be designed right!!!

ANIMAL GENOMICS @ MIZZOU **What Do We Do RIGHT NOW?**

- **Built breed specific tests based upon reduced sets of targeted SNPs that predict genotype at the genes influencing each trait**

Testing 41,028 SNPs in 1,707 Angus Bulls for their association with Marbling
N=509 significant

ANIMAL GENOMICS @ MIZZOU **How Many SNPs Must We Test?**

Testing 41,028 SNPs in 1,707 Angus Bulls for their association with Marbling
N = 57 significant

ANIMAL GENOMICS @ MIZZOU **129 SNPs Explain 59.1% of Marbling Additive Genetic Variation**

ANIMAL GENOMICS @ MIZZOU **31 SNPs Explain 46.13% of AFI Additive Genetic Variation**

AFI: Steer EBVs

698 = Number of animals included in the analysis
 ● = Association of a SNP with the trait of interest
 ▲ = Marker included into the final model for the trait of interest
 46.13% = Percentage of genetic variation in the trait explained by the final model

ANIMAL GENOMICS @ MIZZOU **How Much Of The Variance????**

This process ALWAYS overestimates the amount of variation that will be explained!!!

ANIMAL GENOMICS @ MIZZOU **We Need Independent Validation**

ANIMAL GENOMICS @ MIZZOU **We Genotyped Another 275 Bulls**

Correlations and R² between EPD and MBV for Marbling in the 275 bulls independent validation on bulls.

Model	No. SNPs Selected			
	50	100	150	200
STEP	0.446 (19.9)	0.479 (22.9)	-	-
CCP	0.463 (21.4)	0.524 (27.5)	0.536 (28.7)	0.553 (30.6)
BAYES	0.506 (25.6)	0.567 (32.1)	0.573 (32.8)	0.599 (35.9)
BAYES_CCP	0.509 (25.9)	0.550 (30.3)	0.588 (34.6)	0.596 (35.5)
BAYES_PCR	0.418 (17.5)	0.475 (22.6)	0.487 (23.7)	0.515 (26.5)
BAYES_PLS	0.438 (19.2)	0.474 (22.5)	0.493 (24.3)	0.494 (24.4)
BAYES_RRR	0.390 (15.2)	0.402 (16.4)	0.477 (22.8)	0.518 (26.8)

ANIMAL GENOMICS @ MIZZOU **We Genotyped 698 Steers**

Correlation between marbling MBV and MARB phenotype (accuracy) and amount of additive genetic variance explained (R²) in 698 Angus steers.

Trait	Model	No. SNPs Selected			
		50	100	150	200
MARB (r ² =0.42)	STEP	0.264 (16.5)	0.276 (18.0)		
	CCP	0.258 (15.8)	0.302 (21.6)	0.303 (21.8)	0.311 (22.9)
	BAYES	0.080 (1.5)	0.228 (12.3)	0.372 (32.3)	0.354 (29.7)
	BAYES_CCP	0.278 (18.3)	0.291 (20.0)	0.392 (36.4)	0.431 (44.0)
	BAYES_PCR	0.325 (25.0)	0.234 (13.0)	0.252 (15.3)	0.360 (30.7)
	BAYES_PLS	0.361 (30.9)	0.364 (31.4)	0.268 (17.0)	0.327 (25.3)
	BAYES_RRR	0.264 (16.5)	0.386 (35.3)	0.315 (23.5)	0.391 (36.2)

ANIMAL GENOMICS @ MIZZOU **Conclusion?**

- With 100 SNPs we can explain ~30% of the genetic variance
- What can we achieve with a 384 SNP assay?
 - We can deliver this at a price point that makes the test worthwhile

Correlation between EPD and MBV for a 384 SNP assay optimized in 1,710 Angus bulls and validated in 275 bulls.

Trait	Correlation	R ²
MARB	0.594	35.3
BFAIT	0.321	10.3
REA	0.575	33.1
CWT	0.455	18.9
HPG	0.386	14.9
YWT	0.348	12.1

Correlation between MBV and phenotype for marbling and rib-eye muscle area (accuracy) and proportion of additive genetic variance explained for an optimized 384 SNP assay in 698 Angus steers.

Trait	h ²	Accuracy	R ²
MARB	0.425	0.485	55.3
REA	0.311	0.434	60.6

ANIMAL GENOMICS @ MIZZOU **Conclusions**

- Because of the importance to the industry of these first BovineSNP50 derived tests, Merial and Missouri performed an external validation with ISU to confirm marker effects and % genetic variation explained
- Merial will soon have available a commercial product for Angus, built from these data and validated in commercial steers and registered Angus sires
- Merial and AGI are working to incorporate other Angus-specific products into their national genetic evaluation, and genomic EPDs will soon be available to cattlemen from reduced SNP panels and the BovineSNP50 assay

ANIMAL GENOMICS @ MIZZOU **What About Other Breeds?**

- We have genotyped Limousin, Charolais, Hereford, Simmental and are working on across-breed tests
 - It would be really helpful if someone set up a Beef DNA Repository
- May require a 1 Million SNP assay
 - About 1 year away
- It's time we begin to produce difficult but expensive phenotypes on the most important traits...because Genomic Selection is here!!!!
 - Disease resistance, meat palatability, etc...

The End

