


Whole Genome Scanning for the Beef Industry



iDon'tTreadInIt™ Custom Cow Chip
Photo Courtesy Jim Womack

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Outline

- Brief history of gene mapping in beef cattle
- Why do we have so few tests?
- What lessons have we learned along the way?
- High density SNP genotyping to the rescue!
 - New approaches to genetic improvement
 - New strategies for the development of tests
 - 48K Illumina iSelect Bovine Chip
- Applications
 - Data from 518/2,641 cattle SNPs



It may be what's for dinner... but we don't know much about beef quality until we eat it!!

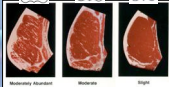





July 1 U.S. Cattle Inventory 1973-2001

The 2001 annual gross sale of 11.8 million feedlot cattle was \$36.8 billion and the total value of the national herd was \$70.6 billion

Beef QTL Mapping (Quantitative Trait Locus)

- 1990 – Three growth & meat quality QTL programs
 - CSIRO - Halfsib design *Bos taurus* × *Bos indicus* F₁ bulls
 - USMARC – Halfsib design *Bos taurus* × *Bos indicus* F₁ bulls
 - TAMU - Fullsib design *Bos taurus* × *Bos indicus* F₂ and reciprocal backcross families
- Why *Bos indicus* vs *Bos taurus*?
 - Phenotypically extreme for meat quality (marbling and tenderness)
 - Last Common Ancestor 200-500 Kya
 - Maximize likelihood of detecting QTL of large effect if they existed!!

Identified QTL!!!

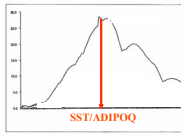
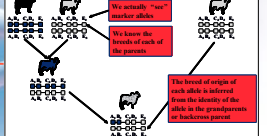
400 markers x 700 individuals = 250K genotypes
4-5 QTL/trait - frequently inconsistent across studies

Experimental Design


Effect of Recombination

Marker/Phenotype associations reveal QTL

DNA markers detect parent and breed of origin

But Not Many QTN! (Quantitative Trait Nucleotides)

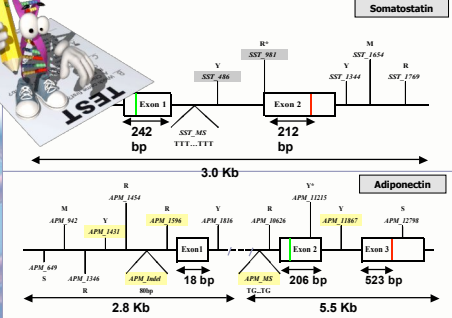


Somatostatin

Exon 1: 242 bp
Exon 2: 212 bp
3.0 Kb region

Adiponectin

Exon 1: 18 bp
Exon 2: 206 bp
Exon 3: 523 bp
2.8 Kb region



Why Not?

(Lessons #1, 2 and 3)

1) Fixed allelic difference every 300 bp between *Bos indicus* and *Bos taurus* causal differences nonidentifiable

2) Any QTL that is experimentally detectable will be segregating in all *Bos taurus* breeds

3) We should be mapping in commercially and phenotypically relevant populations

Why Not?

(Lessons #4 and 5)

4) Without a whole genome sequence it is extremely difficult to identify markers for fine mapping, identify positional candidate genes and resequence these genes to identify putative causal mutations

5) It also means that there are essentially no SNPs and that all mapping studies are microsatellite-based

- Limits mapping resolution (#markers scored)
- Limits # of individuals typed (cost and sample logistics)

Lesson 6

Mapping in halfsib - families

1. Mapping in halfsib families establishes sire QTL genotype

This sire is segregating for a QTL near the second marker on BTA14

But you need a large number of families to ensure that you have 2 or 3 families segregating for each QTL

This sire is not segregating for a QTL anywhere on BTA14

Lesson 6

Mapping in halfsib - families

2. A large number of families will capture the diversity within a population (rare variants) - but likely to be interpreted as false positives

3. Halfsib families differentiate pleiotropic vs closely linked QTL

4. Halfsib families allow statistical inference of causality

9 sires heterozygous for ADIPOQ indel

A Really Big Microsatellite Study

- Registered Angus (AI)
 - 1,768 bulls via semen
 - EPDs and accuracies for 17 growth and carcass traits on 23,000 relatives provided by AAA
- Circle A Ranch
 - 5,344 steers (2,197 genotyped)
 - 39 families (HS)
 - Growth, carcass and ultrasound measurements
 - ~600 With feed intake and RFI
 - ~200 with RFI from MFA
 - 422 Microsatellites
 - 3,965 animals
 - 1.6 M genotypes

How Many Marbling QTL?

Segregating Sires

Marbling QTL

Chromosome-wide P < 0.05
Genome-wide P < 0.05

Bos Taurus Chromosome

59 at Genome-wide P ≥ 0.05
Two per chromosome!

17 previously reported (small study sampling effects)
AAA publishes genetic evaluations for 17 traits
17 traits x 60 QTL = 1,020 QTL

How Are We Going To Make Tests For All These QTL?

Bull's Genome
30 pairs of chromosomes ~ 30,000 genes
Marbling genes

The concept of **Whole Genome Selection** is that we use a very high resolution map (50K markers) to divide the genome into small segments (haplotypes) and estimate the contribution of each haplotype and chromosomal segment to genetic merit

Whole Genome Selection

- Advantages
 - Simultaneously test for all genes and all traits
- Disadvantages?
 - Every breed will have to do its own discovery analyses
 - We (probably) won't get close enough to a feed efficiency gene in Angus steers for the test to work in Hereford
 - We don't know how long (generations) predictive power will hold up
- Is there a back-up plan?

How Do We Find The Genes If WGS Doesn't Work?

- Whole genome sequence the parents (Solexa/454/Helicos)
- Align sequences and identify concordant mutations for ALL QTLs for EVERY trait
- Current cost ~\$300K/14X genome (soon \$100K)

May represent animals from multiple breeds (patterns of LD)

- But can we assemble it?
- And how do we refine the regions of interest?

Lesson 7

No more microsatellite genotyping!

- Formed consortium to develop 48,000 SNP Illumina iSelect® assay
- Curt van Tassell (BARC), Tad Sonstegard (BARC), Tim Smith (MARC), Steve Moore (Alberta), Jerry Taylor (Missouri), Bob Schnabel (Missouri)
- 60,800 tags – guarantee 48,000 SNPs convert
- Plan to genotype ~24,000 animals for multiple projects

Association analysis of 518 SNPs in 68 Angus bulls with Marbling EPD Accuracy >0.05

So...What Populations Are Available For Gene Discovery?

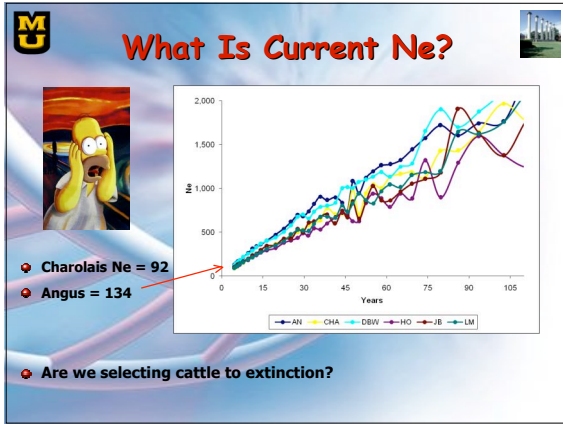
- 1,768 Registered Angus Bulls (17 traits)
- 5,484 Circle A Angus Steers (15 traits)
- 813 Angus Steers with RFI
- 6,245 Registered Limousin (13 Traits)
- ~5,000 Carcass Merit Project Steers (15 traits)

Breed	# Steers	# Programs	Av. # Programs	N _e	Min. # Prog.	Max. # Prog.
Angus	28	353	12.6	3,250.1	2	35
Charolais	33	720	21.8	12,099.9	2	53
Simmental	39	700	18.0	15,283.9	2	55
Simmental*	94	960	10.2	12,024.0	1	28
Simmental*	14	350	25.0	10,033.0	3	47
Hereford	69	1,264	18.3	27,286.6	1	43
Limousin	277	4,547	15.7	83,299.1	1	55

- Angus
- Charolais
- Hereford
- Limousin
- Simmental/Simbrah

What Is The Effective Population Size (Ne) of Beef Cattle Breeds?

- $E[r^2] = 1/(1+4NeD)$ Sved (1971)
- Ne is population size 1/2D generations ago Hayes et al. (2003)
- 2,641 SNPs, 8 breeds, 43-96 animals/breed



Acknowledgements

Angus Resources

- Dr. Scott Barao – Semen on 221 Wye Plantation bulls
- Accelerated Genetics, SEK Genetics, Select Sires, Genex, ABS
- Greg Jorgensen – 1100 samples
- Numerous Angus breeders - semen
- Gary Johnson
- David Gust Family & Circle A Ranch
- American Angus Association

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