Slide 1

Improving Genetic Prediction for Beef Cattle – Lessons Learned from Dairy Cattle

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AIPL – Animal Improvement Programs Laboratory
BFGL – Bovine Functional Genomics Laboratory

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Trends in U.S. Milk Production
Selection Works

In 2007 U.S. Produced 34% more milk with 48% fewer dairy cows than in 1960

Slide 3
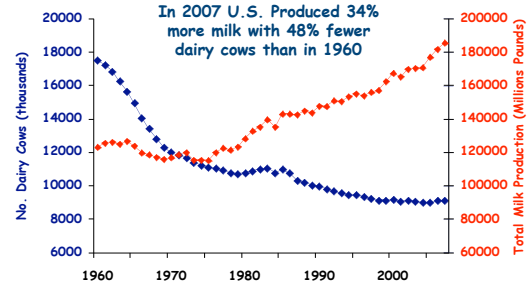
Traditional Selection Programs

- Collect phenotypic data from animals (e.g., milk production, growth rate, conformation,etc.)
- Estimate genetic merit for animals in a population
- Select superior animals as parents of future generations

Phenotype
Pedigree
Statistical Methodology
Predicted Genetic Merit

Slide 4
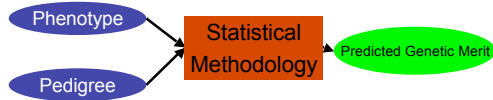
Cattle SNP Collaboration iBMAC

- Developed 54,001 SNP Illumina assay
  - USDA-ARS Beltsville Agricultural Research Center: Bovine Functional Genomics Laboratory and Animal Improvement Programs Laboratory
  - University of Missouri
  - University of Alberta
  - USDA-ARS US Meat Animal Research Center
- Consortium planned to genotype ~30,000 animals for multiple projects

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Participants

iBMAC Consortium	Funding Agencies
Illumina	USDA/NRI/CSREES
· Marylinn Munson	· 2006-35616-16697
· Cindy Lawley	· 2006-35205-16888
· Christian Haudenschild	· 2006-35205-16701
BARC	USDA/ARS
· Curt Van Tassell	· 1265-31000-081D
· Lakshmi Matukumalli	· 1265-31000-090D
· Tad Sonstegard	· 5438-31000-073D
Missouri	Merial
· Jerry Taylor	· Stewart Bauck
· Bob Schnabel	NAAB
· Stephanie McKay	· Godon Doak
Alberta	· ABS Global
· Steve Moore	· Accelerated Genetics
USMARC – Clay Center	· Alta Genetics
· Tim Smith	· CRI/Genex
· Mark Allan	· Select Sires
	· Semex Alliance
	· Taurus Service

Slide 6

USDA-ARS project – Initiated 2006

- Genotype 3,000 to 5,000 Holsteins
  - Built in validation
    - Historic group
      - 2000 bulls born in 1995-1997
      - 400 ancestor bulls born in 1950-1994
    - Prediction group
      - 800-1000 bulls born in 2001-2002
  - Test ability to predict "forward"
- Genotype 750-1000 Jerseys
- Genotype 250-400 Brown Swiss
- Depended on CDDR
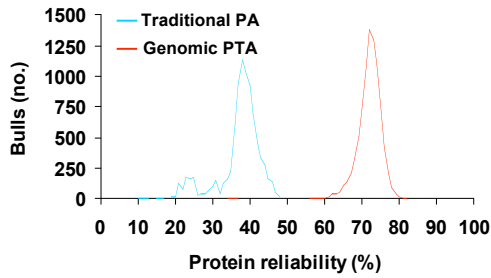
Population Structure
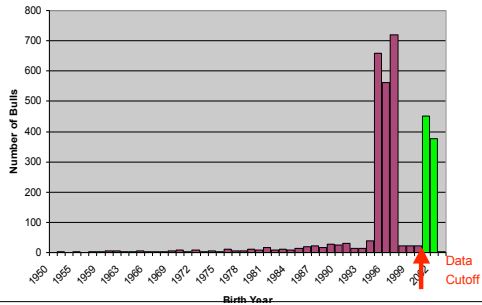
Reliability Gain[1] by Breed
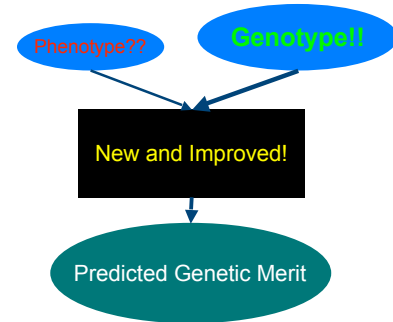
Yield traits and NM$ of young bulls

Trait	HO	JE	BS
Net merit	23	9	3
Milk	23	11	0
Fat	33	15	5
Protein	22	4	1
Fat %	43	41	10
Protein %	34	29	5

[1]Gain above parent average reliability ~35%

Reliabilities for Young Bulls

Build a Better Black Box

Phenotype??　　Genotype!!

New and Improved!

Predicted Genetic Merit

Problems…

- Upper limit on accuracy of genetic prediction – even for Holstein
- What do we do with smaller breeds – marker effects were not consistent enough to justify across-breed genetic prediction

Development of a Bovine High-Density SNP Assay

- Why?
  - Increased accuracy in genetic prediction
  - Utilize across breed information
  - Enhance gene mapping precision
  - Enhanced performance in *Zebu* cattle

Collaboration

- Illumina provided:
  - DNA sequence for a range of breeds
- Pfizer provided:
  - DNA sequence of additional breeds
  - SNP discovery expertise
- USDA-ARS provided:
  - DNA and library construction
  - SNP discovery expertise
  - Assay design expertise

Additional Collaborators

- University of Missouri
- Roslin Institute
- UNCEIA (France)
- Sao Paulo State University
- University of Milan
- Technische Universitaet Muenchen
- Beef CRC
- Embrapa
- National University (Korea)

Data Highlights

- Enormous amount of DNA sequence data
  - ~180x genome equivalent coverage
  - ~550 **BILLION** base-pairs
- Represents:
  - ~120 libraries
  - >300 animals
- Animals from breeds representing:
  - European and Zebu cattle
  - Beef and dairy
 - Temperate and tropically adapted

SNP Chip Design

- >45 million SNPs discovered
- ~6 million were used to design the high density chip
  - Selected ~800,000 new SNPs added
  - Kept all of the BovineSNP50 SNPs
- Breed groups used:
  - Holstein, Angus, Nelore, Taurine dairy, Taurine beef, Indicine, tropically adapted Taurine
- 852,645 total gaps
  - 850,816 <20kb
  - 1795 >20kb, < 100kb
  - 34 > 100 kb

Assay Design Results

- All of BovineSNP50 SNP were attempted
- ~800,000 bead types after 60,800 beads of BovineSNP50 positioned
- 795,000 SNP positioned on BTA1-29,X
- 5,000 beads represent unknown contigs, BTA Y, and mitochondrial SNP

Gaps <20,000 bp
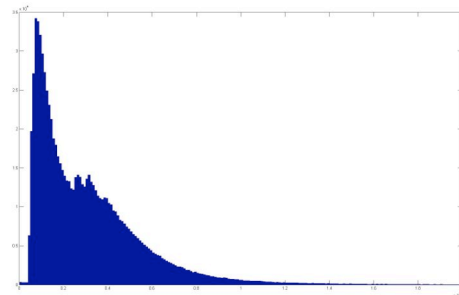
Conclusions

- The Illumina BovineHD genechip will be available *very* soon
- The information from this DNA chip looks very promising for a wide range of uses
- A large number of SNP have been discovered and will be made publically available

Low Density Assay

- What?
  - 96, 384, 1,500, 3,000, ….
- Why?
  - Parentage
    - 10 to 30% incorrect parentage
  - Traceability
    - Disease outbreak
  - Genetic Prediction
    - Intermediate accuracy
  - Shortcut to pedigree data

Reduced SNP Set

- Collaboration
  - Illumina
  - Genomics companies - Merial, Pfizer, MMI
  - Artificial insemination organizations
  - Breed associations
  - Genotyping service providers
  - Eartag manufacturers

- Technology applicable to extensive management practices.

Bull – MGS Relationships
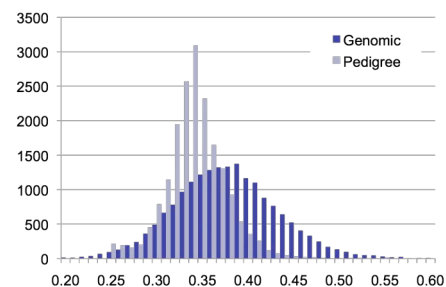
What is imputation?

- Prediction of unknown genotypes from observed genotypes
  - Pedigree haplotyping
  - Matching allele patterns
- Genotypes indicate how many copies of each allele were inherited
- Haplotypes indicate which alleles are on which chromosome

Why impute haplotypes?

- Predict dam from progeny SNP
- Predict unknown SNP from known
  - Measure 3,000, predict 50,000 SNP
  - Measure 50,000, predict 850,000
  - Measure each haplotype at highest density only a few times
- Increase reliabilities while minimizing costs – $40 vs $225 vs $325
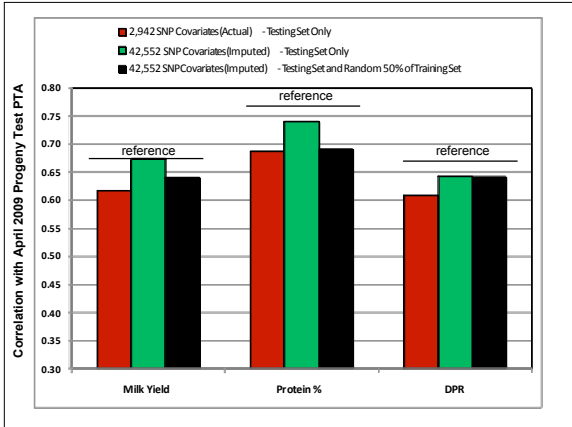
Correlations of 3K and PA with 50K

Trait	Corr(3K,50K)^2	Corr(PA,50K)^2	Gain
NM$	.899	.518	79%
Milk	.920	.523	83%
Fat	.920	.516	83%
Prot	.920	.555	82%
PL	.933	.498	87%
SCS	.912	.417	85%
DPR	.937	.539	86%

Genomic Pedigree!!
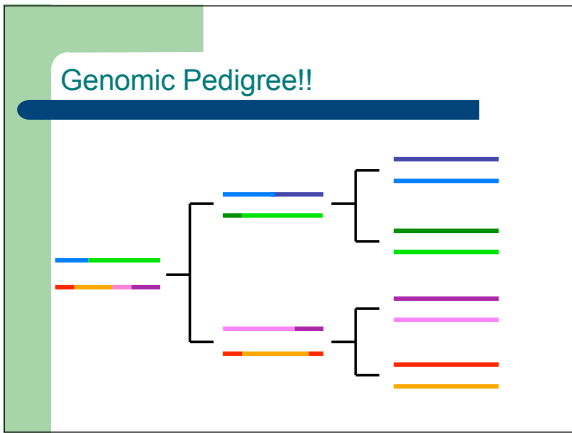
Conclusions

- Genomics is radically altering dairy cattle breeding
- We are collaboratively developing tools to increase the ability to characterize cattle with very high density SNP chips
- We are developing with industry partnerships to bring this technology to the producer level
  - This technology has the potential to impact the developing world

iBMAC Consortium	Implementation Team	Funding
• Illumina (industry) – Marylinn Munson – Cindy Lawley – Diane Lince – LuAnn Glaser – Christian Haudenschild • Beltsville (USDA-ARS) – Curt Van Tassell – Lakshmi Matukumalli – Steve Schroeder – Tad Sonstegard • Univ Missouri (Land-Grant) – Jerry Taylor – Bob Schnabel – Stephanie McKay • Univ Alberta (University) – Steve Moore • Clay Center, NE (USDA-ARS) – Tim Smith – Mark Allan	• AIPL – Paul VanRaden – George Wiggans – John Cole – Leigh Walton – Duane Norman • BFGL – Marcos de Silva – Tad Sonstegard – Curt Van Tassell – University of Wisconsin – Kent Weigel – University of Maryland School of Medicine – Jeff O'Connell – Partners – GeneSeek – DNA Landmarks – Expression Analysis – Genetic Visions	• USDA/NRI/CSREES – 2006-35616-16697 – 2006-35205-16888 – 2006-35205-16701 • USDA/ARS – 1265-31000-081D – 1265-31000-090D – 5438-31000-073D • Merial – Stewart Bauck • NAAB – Gordon Doak – Accelerated Genetics – ABS Global – Alta Genetics – CRI/Genex – Select Sires – Semex Alliance – Taurus Service