Genomic selection in the USA

George Wiggans, Technical Advisor
george.wiggans@uscdcb.com
Council on Dairy Cattle Breeding
www.uscdcb.com
Highlights of U.S. system

- Nearly 700,000 animals genotyped in 2018
- 67% of AI breedings to genomic bulls
- Genomic relationship between genotyped cows and marketed bulls provided to avoid matings that result in high inbreeding
- Evaluations of all animals updated monthly
- Evaluations on new animals released weekly
Government–industry collaboration

• Animal Genomics and Improvement Laboratory (AGIL), Agricultural Research Service, U.S. Department of Agriculture (USDA)
  • Responsible for research and development to improve the evaluation system
  • Located in Beltsville, Maryland

• Council on Dairy Cattle Breeding (CDCB)
  • Responsible for approving changes, receiving data, and computing and delivering U.S. genetic evaluations for dairy cattle
  • Located in Bowie, Maryland
Funding

- CDCB evaluation calculation and dissemination funded by fee system
  - Based on animals genotyped
  - ~66% of revenue from bulls
  - Credits for herds that contribute more information

- USDA research on evaluation methodology funded by U.S. Federal Government
U.S. dairy genomics history

- Dairy DNA repository (Canada, U.S.) 1992
- Cattle genome sequenced 2004
- Illumina 50K SNP BeadChip 2007
- Official genomic evaluations (Holstein, Jersey, Brown Swiss) 2009
- High-reliability, low-density chip 2011
- Genomic evaluations transferred from USDA to CDCB 2013
Council on Dairy Cattle Breeding (CDCB)

- 3 members from each organization
- Total of 12 voting members
- 2 nonvoting industry members
Genomic data flow

Animal manager/owner

DNA laboratory

DNA samples

AI organization, breed association

genotypes

nominations, pedigree data

genomic evaluations

Council on Dairy Cattle Breeding (CDCB)

genotypes

genotype quality reports

DNA samples

DNA samples

genomic evaluations

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DNA source – samples sent to genotyping labs (2018)

<table>
<thead>
<tr>
<th>Source</th>
<th>Samples (no.)</th>
<th>Samples (%)</th>
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<tbody>
<tr>
<td>Blood</td>
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<td>2</td>
</tr>
<tr>
<td>Hair</td>
<td>102,229</td>
<td>14</td>
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<tr>
<td>Nasal swab</td>
<td>656</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Semen</td>
<td>319</td>
<td>&lt;1</td>
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<tr>
<td>Tissue</td>
<td>579,255</td>
<td>81</td>
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<tr>
<td>Unknown</td>
<td>17,048</td>
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</table>
Laboratory quality control

- Each SNP evaluated for
  - Call rate
  - Portion heterozygous
  - Parent-progeny conflicts

- Clustering investigated if SNP exceeds limits

- Number of failing SNPs indicates quality of submission

- PASS/FAIL report on 7 conditions sent to labs
Before clustering adjustment

86% call rate
After clustering adjustment

100% call rate
Genotype counts by chip density (2018)

- 9K: 126,183
- 18K: 5,174
- 27K: 498,271
- 47K: 49,739
- 53K: 1,750
- 60K: 12,875
- 138K: 4,742
- 773K: 901

Genotypes (no.)

Chip density

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Usable genotype counts by animal sex

- **Bulls**
- **Cows**

Genotypes (no.)

Year first genotype received

### International genotype exchanges

<table>
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<th>Country exchanges with U.S.</th>
<th>Breed</th>
<th>Sex</th>
<th>Since</th>
</tr>
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<tbody>
<tr>
<td>Canada</td>
<td>All</td>
<td>Both</td>
<td>2009</td>
</tr>
<tr>
<td>United Kingdom, Italy</td>
<td>Holstein</td>
<td>Bulls</td>
<td>2011</td>
</tr>
<tr>
<td>All Europe via Interbull</td>
<td>Brown Swiss</td>
<td>Bulls</td>
<td>2012</td>
</tr>
<tr>
<td>Denmark</td>
<td>Jersey</td>
<td>Bulls</td>
<td>2014</td>
</tr>
<tr>
<td>United Kingdom (1 time)</td>
<td>Guernsey</td>
<td>Both</td>
<td>2014</td>
</tr>
<tr>
<td>Japan, Switzerland, Germany</td>
<td>Holstein</td>
<td>Bulls</td>
<td>2016</td>
</tr>
</tbody>
</table>
Genotyped animals in database by region (2018)

- North America: 2,585,255
- South America: 27,356
- Europe: 7,749
- Africa: 23,408
- Asia: 200,002
- Oceania: 18,513

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Validation of parents

- Around 3 million animals genotyped in U.S. system
- Portion of parents validated
  - 97% of sires
  - 39% of dams
- Each genotype compared with all others to discover identical genotypes and parent-progeny relationships
- Animals with incorrect sire or dam excluded from evaluation
Parentage validation and discovery

- Parent-progeny conflicts detected
  - Reported to breeds and requesters
  - Correct sire usually detected
Imputation

• Based on splitting genotype into individual chromosomes (maternal and paternal contributions)

• Missing SNPs assigned by observing SNPs in ancestors and descendants

• Enables use of lower cost/fewer SNP chips

• Genotypes from all chips merged by imputing SNPs not present
Gene tests (imputed and actual)

- Holstein
  - Bovine leucocyte adhesion deficiency (BLAD)
  - Complex vertebral malformation (CVM)
  - Deficiency of uridine monophosphate synthase (DUMPS)
  - Syndactyly (mulefoot)
  - Cholesterol deficiency
  - Red coat color

- Brown Swiss
  - Weaver Syndrome
  - Spinal dismyelination (SDM)
  - Spinal muscular atrophy (SMA)

- Polledness (Holstein, Jersey, Brown Swiss)
Haplotypes affecting fertility

- Rapid discovery of new recessive defects
  - Large numbers of genotyped animals
  - Affordable DNA sequencing

- Determination of haplotype location
  - Significant number of homozygous animals expected, but none observed
  - Narrow suspect region with fine mapping
  - Use sequence data to find causative mutation
## Haplotypes affecting fertility

<table>
<thead>
<tr>
<th>Name</th>
<th>Chromosome</th>
<th>ARS-UCD location (Mbp)</th>
<th>Current carrier frequency (%)</th>
<th>Earliest known genotyped ancestor</th>
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<tbody>
<tr>
<td>HH1</td>
<td>5</td>
<td>62.8*</td>
<td>2.6</td>
<td>Pawnee Farm Arlinda Chief</td>
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<tr>
<td>HH2</td>
<td>1</td>
<td>93.5–95.6</td>
<td>2.4</td>
<td>Willowholme Mark Anthony</td>
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<tr>
<td>HH3</td>
<td>8</td>
<td>93.8*</td>
<td>5.3</td>
<td>Glendell Arlinda Chief, Gray View Skyliner</td>
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<tr>
<td>HH4</td>
<td>1</td>
<td>2.0*</td>
<td>0.5</td>
<td>Besne Buck</td>
</tr>
<tr>
<td>HH5</td>
<td>9</td>
<td>91.8–91.9</td>
<td>4.8</td>
<td>Thornlea Texal Supreme</td>
</tr>
<tr>
<td>HH6</td>
<td>16</td>
<td>29.0–29.1</td>
<td>0.9</td>
<td>Gray View Skyliner</td>
</tr>
<tr>
<td>JH1</td>
<td>15</td>
<td>15.4*</td>
<td>18.4</td>
<td>Observer Chocolate Soldier</td>
</tr>
<tr>
<td>BH2</td>
<td>19</td>
<td>10.8*</td>
<td>13.3</td>
<td>Rancho Rustic My Design</td>
</tr>
<tr>
<td>AH1</td>
<td>17</td>
<td>63.7*</td>
<td>22.3</td>
<td>Selwood Betty’s Commander</td>
</tr>
<tr>
<td>AH2</td>
<td>3</td>
<td>51.1</td>
<td>13.3</td>
<td>Oak-Ridge Flashy Kellogg</td>
</tr>
</tbody>
</table>

1BH1 and JH2 discontinued  
2*Bos taurus* (BTA)  
3Mbp = megabase pairs; * = causative mutation known
Detection of chromosomal abnormalities

• Location of conflicts checked if parent and progeny have more conflicting SNPs than allowed for true parent-progeny relationship

• Parent-progeny relationship accepted if conflicts concentrated on single chromosome
  • Large deletion – animal homozygous in the region
  • Uniparental disomy – heterozygous SNPs in the region
  • 152 cases discovered so far
Validation of grandsires

- Grandsire checked if parent not genotyped or not confirmed
- Grandsire declared unlikely if animal and grandsire have more opposite homozygotes than threshold percentage (declines as possible comparisons increase)
- Possible grandsires suggested if low percentage of conflicts and birth date reasonable
- Animals with unlikely grandsires excluded from evaluation
Use haplotypes for MGS discovery

• Include new animals with unknown or unlikely MGS in weekly evaluation calculations (confirmed sire required)

• Blank conflicting pedigree and suppress release of evaluation for genotypes not qualifying for evaluation

• Only 1 SNP-at-a-time detection of opposite homozygotes available for paternal grandsire
Heritabilities used in U.S. genetic evaluation

<table>
<thead>
<tr>
<th>Trait</th>
<th>Heritability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield (milk, fat, protein)</td>
<td>15–29</td>
</tr>
<tr>
<td>Conformation (type, ~17 traits)</td>
<td>8–51</td>
</tr>
<tr>
<td>Longevity (productive life, cow livability)</td>
<td>1.3–8</td>
</tr>
<tr>
<td>Somatic cell score (mastitis resistance)</td>
<td>12</td>
</tr>
<tr>
<td>Daughter pregnancy rate</td>
<td>1.4</td>
</tr>
<tr>
<td>Heifer conception rate</td>
<td>1</td>
</tr>
<tr>
<td>Cow conception rate</td>
<td>1.6</td>
</tr>
<tr>
<td>Service sire (direct) calving ease</td>
<td>8.6</td>
</tr>
<tr>
<td>Daughter (maternal) calving ease</td>
<td>4.8</td>
</tr>
<tr>
<td>Service sire (direct) stillbirth rate</td>
<td>0.8</td>
</tr>
<tr>
<td>Daughter (maternal) stillbirth rate</td>
<td>2.1</td>
</tr>
<tr>
<td>Gestation length (heifers, cows)</td>
<td>44–48</td>
</tr>
<tr>
<td>Age at first calving (early maturity)</td>
<td>2.7</td>
</tr>
<tr>
<td>Health (hypocalcemia, displaced abomasum, ketosis, mastitis, metritis, retained placenta)</td>
<td>0.6–3.1</td>
</tr>
</tbody>
</table>
## Dairy cattle traits evaluated by CDCB

<table>
<thead>
<tr>
<th>Year</th>
<th>Trait</th>
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<tbody>
<tr>
<td>1926</td>
<td>Milk &amp; fat yields</td>
</tr>
<tr>
<td>1977</td>
<td>Protein yield (&amp; solids-not-fat)</td>
</tr>
<tr>
<td>1978</td>
<td>Conformation (type)</td>
</tr>
<tr>
<td>1994</td>
<td>Productive life, somatic cell score (mastitis resistance)</td>
</tr>
<tr>
<td>2000</td>
<td>Calving ease (Iowa State University, 1978–99)</td>
</tr>
<tr>
<td>2003</td>
<td>Daughter pregnancy rate</td>
</tr>
<tr>
<td>2006</td>
<td>Stillbirth rate, bull conception rate (ERCR, DRMS, Raleigh, NC, 1986–2005), milking speed</td>
</tr>
<tr>
<td>2009</td>
<td>Cow and heifer conception rates, <strong>genomic evaluation</strong></td>
</tr>
<tr>
<td>2012</td>
<td>Mobility, calving-to-insemination interval</td>
</tr>
<tr>
<td>2016</td>
<td>Gestation length</td>
</tr>
<tr>
<td>2017</td>
<td>Cow livability</td>
</tr>
<tr>
<td>2018</td>
<td>Health traits (milk fever, displaced abomasum, ketosis, mastitis, metritis, retained placenta)</td>
</tr>
</tbody>
</table>
Evaluation of new traits

• Early first calving – April 2019
  • Calculated from age at first calving
  • Higher values mean earlier calving

• Feed efficiency – Under development
Application to more traits

- Animal’s genotype good for all traits
- Traditional evaluations required for accurate estimates of SNP effects
- Traditional evaluations not currently available for heat tolerance or feed efficiency
- Research populations could provide data for traits that are expensive to measure
- Will resulting evaluations work in target population?
Recent changes

• Increase from 60,000 to 80,000 SNPs used in evaluation – December 2018

• Evaluation of crossbreds by blending purebred SNP effects – April 2019

• New fee schedule – April 2019
Evaluation of crossbreds

• Breed proportions called breed base representation (BBR) estimated as 5 genomic traits (Ayrshire, Brown Swiss, Guernsey, Holstein, Jersey) from purebred animals

• Animals with highest BBR < 90 evaluated by applying SNP effect solutions from each breed and then weighting by BBR

• Reference population limited to BBR ≥ 94

• Type, calving, and health traits not blended because not comparable or not available for all breeds
Release of evaluations

• Download from CDCB FTP site with separate files for each nominator

• Weekly release of evaluations of new animals

• Monthly release for females and bulls not marketed

• All genomic evaluations updated 3 times each year with traditional evaluations
Inbreeding for Holstein cows

- Inbreeding
- Expected future inbreeding
AI breedings to genomic bulls

**Holstein service sires**
- Old, nongenotyped
- Old, genotyped
- 1st crop, nongenotyped
- 1st crop, genotyped
- Young, nongenotyped
- Young, genotyped

<table>
<thead>
<tr>
<th>Breeding year</th>
<th>Old, nongenotyped</th>
<th>Old, genotyped</th>
<th>1st crop, nongenotyped</th>
<th>1st crop, genotyped</th>
<th>Young, nongenotyped</th>
<th>Young, genotyped</th>
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<tr>
<td>2011</td>
<td>48</td>
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<td>0</td>
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<tr>
<td>2012</td>
<td>51</td>
<td>8</td>
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<td>0</td>
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<tr>
<td>2013</td>
<td>54</td>
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<td>0</td>
<td>0</td>
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<td>2014</td>
<td>58</td>
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<td>2015</td>
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<td>2016</td>
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<td>2018</td>
<td>67</td>
<td>2</td>
<td>0</td>
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Genetic merit of marketed Holstein bulls

Average gain: $16.25/year

Average gain: $44.00/year

Average gain: $77.57/year
Net merit of active AI and genomic bulls

- Holstein active AI bulls
- Holstein genomic bulls
- Jersey active AI bulls
- Jersey genomic bulls

Bull birth year:
- 2012
- 2013
- 2014
- 2015
- 2016
- 2017

Reliability (%):
- 0
- 20
- 40
- 60
- 80
- 100

Net merit ($):
- 0
- 200
- 400
- 600
- 800
- 1,000

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## Genetic-economic index changes across time

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<td>−1</td>
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<td>Fat</td>
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<td>46</td>
<td>25</td>
<td>21</td>
<td>22</td>
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<td>22</td>
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<td>Health$</td>
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<td>...</td>
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</tbody>
</table>
Relative weighting in 2018 net merit (NM$)

- UC  Udder composite
- BWC  Body weight composite
- FLC  Feet-legs composite
- DPR  Daughter pregnancy rate
- CCR  Cow conception rate
- HCR  Heifer conception rate
- CA$  Calving ability (calving ease & stillbirth rate)
- PL  Productive life
- LIV  Livability
- SCS  Somatic cell score
- MAST  Mastitis
- METR  Metritis
- DA  Displaced abomasum
- RETP  Retained placenta
- KETO  Ketosis
- MFEV  Milk fever

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What we expect in the future

• Increasing number of cows genotyped
• Falling cost per SNP genotyped
• Increased accuracy of genomic evaluations from more informative SNPs
• Genomic evaluations on more traits to predict economic merit more accurately
• Increased use of genomics in mating programs
Why genotype females?

• Improve accuracy of culling and breeding decisions

• Breeding
  • Cows to flush
  • Cows to breed with sexed semen
  • Cows to breed to beef bulls

• Improved avoidance of inbreeding

• More accurate culling
Benefits of genomics

- Determine genetic merit of animals at a young age
- Increase selection intensity
- Increase accuracy of selection
- Reduce generation interval
- Increase rate of genetic gain
- Identify genetic defects and reduce their frequency
- Parentage discovery
- Herd management
  - Cull low-end replacement animals earlier
  - Breed lower merit animals to beef bulls
Summary

• U.S. genetics recognized and used around the world as “the source” in many breeding programs
• Largest genetic base and high selection intensity produces elite bulls and cows
• Genomics revolutionized animal breeding
• International collaboration important to program success
Acknowledgments & disclaimers

• Research support funded through USDA-ARS project 8042-31000-002-00, “Improving dairy animals by increasing accuracy of genomic prediction, evaluating new traits, and redefining selection goals”

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