Genetic Gain Full Throttle – Acceleration of genetic improvement through today’s technologies

M. Allan
Trans Ova Genetics

Genetic Gain Full Throttle - Acceleration of genetic improvement through today’s technologies

Dr. Mark Allan
Director Marketing and Genomics
Trans Ova Genetics

Forward-Looking Statements

Some of the statements made in this presentation are forward-looking statements. These forward-looking statements are based upon our current expectations and projections about future events and generally relate to our plans, objectives and expectations for the development of our business.

Although management believes that the plans and objectives reflected in or suggested by these forward-looking statements are reasonable, all forward-looking statements involve risks and uncertainties and actual future results may be materially different from the plans, objectives and expectations expressed in this presentation. All information in this presentation is as of the date marked on the cover page, and Trans Ova Genetics undertakes no duty to update this information unless required by law.
The Toolbox

- Sorted Semen
- Recipient Solutions
- In Vitro Fertilization
- Genetic Resources
- Embryo Transfer
- Cloning
- Artificial Insemination
- Precision Breeding
  - Gene Editing

Reproductive Toolbox
Why use ART?

- Assisted reproduction tools coupled with Genomic Selection will accelerate: **genetic gain 2X – 8X**
  - AI started in 1950’s
  - ET started in 1970’s
  - IVF started in 1990’s
  - GP/Cloning started in 1990’s
  - SS started in 2000’s

\[
GG = \frac{\text{Var} \times \text{Acc} \times \text{Selection Intensity}}{\text{Gen. Interval}}
\]

Why Utilize These Tools?

Get More Calves from those Great Cows and Great Sires!
• IVF provides embryo production on open, pregnant, subfertile and pre-puberal females
• Best place to use Sexed Semen
• *More than one calf per year out of those really good cows and heifers*
• ....of the sex you desire most.
Sexed Semen

- Semen can be Sexed/Sorted.
- Over 90% accuracy for sex
- Reverse sorted semen for IVF

Today’s Elite Genetic Selection

1) Qualify donors via high density genomic chips
2) Collect juvenile donors
3) IVF with sexed/conventional semen
4) Gestate all embryos
Today’s Elite Genetic Selection

1) Qualify donors via high density genomic chips

2) Collect juvenile donors

3) IVF with sexed/conventional semen

4) Gestate all embryos

Centers & Satellites
Taking IVF to the Client

Regional IVF Center
TOG OPU team

Impact on production

Embryos Processed

<table>
<thead>
<tr>
<th>Month</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Embryos per collection

<table>
<thead>
<tr>
<th>Year</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.0</td>
<td>1.0</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>5.0</td>
<td>6.0</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td>0.0</td>
<td>1.0</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>5.0</td>
<td>6.0</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td>0.0</td>
<td>1.0</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>5.0</td>
<td>6.0</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td>0.0</td>
<td>1.0</td>
<td>2.0</td>
<td>3.0</td>
<td>4.0</td>
<td>5.0</td>
<td>6.0</td>
<td>7.0</td>
</tr>
</tbody>
</table>

- Aspiration
- Flush
What’s Changed

Components of Phenotypic Variation

- Environment
  - Known
  - Unknown
- Genetics
  - Non-Additive
  - Additive

Advancements In Genetic Improvement

Genetic Evaluation Evolution

- Visual appraisal
- Pedigree information
- Pedigree verification
- Performance data
- Progeny values and accuracy
- Bioeconomic indexes
- Genetic tests for simple recessives
- Targeted panels
- High density panels
- Blended evaluations
- Imputation
Distribution of Genetics

Why do we need more information?

- Two full-sib Angus bulls born with the same parent averages

<table>
<thead>
<tr>
<th>Trait</th>
<th>BW</th>
<th>WW</th>
<th>Milk</th>
<th>YW</th>
<th>SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parent Average</td>
<td>4.4</td>
<td>36</td>
<td>19</td>
<td>63</td>
<td>.76</td>
</tr>
</tbody>
</table>

- Progeny records reveal very different bulls
Dairy Genetic Evaluation - Large portion of data commercial industry progeny test data.

Zoetis Clarified
• April 2014 Top Young Genomic Bull List (412 bulls)

• 87% of the top 100 were produced by Trans Ova and it's clients

Industry Trends

Parent ages for marketed Holstein bulls

Genetic merit of marketed Holstein bulls
Genomics Impact on the Dairy Industry?

- Leverage the GE system already in place
- Training population calibration
- Validation of concept of WGS
- Implementation into genetic evaluations

Genotype animals in the evaluation Holstein

June Genotyped all breeds 992,918

https://www.cdcb.us/Genotype/cur_density.html
Genetic Gain

Genetic Gain = \text{acc} \times \text{genetic variation} \times \text{intensity} \times \text{generation interval}

- Race – genetic improvement
- Young Animals

Genetic Copy Later In Time

VIAGEN
Why do Producers Use this Technology?

Maximizing Production from Outliers
- The leading terminal sires/foundation females.

Contributing to the Genetic Pool
- Genetic Outlier that died young.

Eliminating Recessive Genes/Disease Outbreak
- Going back to a "free" founder.

Extending Reach of Rare Genetics
- Proven performer in high demand.

Genetic Preservation and Cloning

Using the Technology to Capitalize on an Elite Bull’s Genotype

- Genetic donor bull was a “lunger”
  - poor semen production
  - poor morphology

- The owners cloned him to produce a healthier version.

- Picture of health with a phenotype to match and he produces more semen than the genetic donor which is also of excellent quality.
**Additional Applications of Biotechnology**

TOG also produces animals with applications in Biomedical:
- Pharmaceutical production in milk
  - Recombinant human albumen
  - Human Antibodies
- Pigs as medical models
- Organ transplant
- Medical devices

**Fetal cell line selection**

<table>
<thead>
<tr>
<th>Process</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advanced reproductive technologies</td>
<td>3 weeks: IVF embryos → Embryo transfer → Collect fetuses</td>
</tr>
<tr>
<td>Genomic selection</td>
<td>Genotyping and genetic merit evaluation → Frozen cell line aliquots → Establish fibroblast cell lines</td>
</tr>
<tr>
<td>Somatic cell nuclear transfer (SCNT)</td>
<td>Fibroblasts with desired genetics are used as SCNT donor cells → Embryo transfer → High genetic merit calves</td>
</tr>
</tbody>
</table>
What’s Next

Genetic Selection – Generation interval reduced

**Embryo selection**
1. Biopsy – freeze embryos
2. Screen embryos - GPTAs, GEPDs (genomic chips)
3. Transfer selected embryos

**Fetal cell line selection**

QUESTIONS?

www.transova.com
www.viagen.com