Genetic Selection of Dairy Cattle for Improved Immunity

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Warsaw, Poland, Sept 1, 2015
Why are dairy health traits so difficult to improve?

- Difficult to improve genetically - low heritability
- Few direct measures of disease in selection indices, Canada just added mastitis in Aug 2014
- Poor data quality & inconsistency in disease diagnosis and recording
- Selection to fight one disease may be counter-productive to other diseases
Disease Trends in Canada 2008-2011

- Cystic ovaries
- Milk fever
- Displaced abomasum
- Ketosis
- Mastitis
- Lameness
- Retained placenta
- Metritis

Canadian National Health Collection System: CDN 2012 - Courtesy of Dr. F. Miglior
Could Genetic Approaches be used to Improve Immunity in Livestock

We focussed on selecting for broad-based disease resistance based on Estimated Breeding Values (EBVs) of immune response traits
Why Focus on the Immune System?

A strong chain of protection against a wide range of pathogens

Selecting for improved immune response the concept behind our research and

High Immune Response Technology
Immuno-Genetic Approach

AMIR – Extracellular
  eg. *E. coli*
  Mastitis

CMIR – Intracellular
  eg. Virus, Mycobacteria
  Johne’s

Adopted from Wilkie, B. and Mallard, B. 1999 Vet Immunol Immunopath 72:231-235
Capture Broad-based Disease Resistance

Performance of Two Tests

CELL-MEDIATED IMMUNE RESPONSE + ANTIBODY-MEDIATED IMMUNE RESPONSE

Photos and figures courtesy of Dr. B. Mallard
The HIR test requires 3 farm visits:

Immunization and sampling takes ~ 5 min/animal

Individuals with a robust and balanced IR are called **High Immune Responders** and the method is identified as the **HIR Technology**.
HIR Classifies Cattle as High, Average Or Low Immune Responders

Selection for Immune Response is Based on Estimated Breeding Values
Significance of being a High Immune Responder

- Decreased occurrence of mastitis, metritis, ketosis, retained placenta
- Less likely to be seropositive for paratuberculosis
- Faster growth rate
- Beneficial associations with herd life and some reproductive traits
- Improved milk and colostrum quality
- Improved response to vaccine
- Better hoof health – digital dermatitis

Benefit #1 - Lower Disease Incidence

IR vs Disease Incidence (Combined Diseases)

Research carried out on 700 cows
In 3,000 cow dairy in North Florida

- 27% less Mastitis
- 17% less Metritis
- 32% less Retained Placenta
- No adverse production effects

Reference - Thompson-Crispi and Mallard et al. 2012 JDS 95:3888
Mastitis Incidence on Canadian Farms

Incidence of clinical mastitis per 100 cow-years by EBV Low, Average and High AMIR

<table>
<thead>
<tr>
<th>PATHOGEN</th>
<th>LOW AMIR (n=86)</th>
<th>AVE AMIR (n=289)</th>
<th>HIGH AMIR (n=83)</th>
<th>ALL COWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli, S. aureus +</td>
<td>30.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>27.9&lt;sup&gt;a&lt;/sup&gt;</td>
<td>17.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>26.3</td>
</tr>
<tr>
<td>others</td>
<td>6.15&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.98&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.13</td>
<td>2.72</td>
</tr>
</tbody>
</table>

Reduction in Mastitis by High AMIR = \(\frac{(26.3 - 17.1)}{26.3} = 35\%\)

Incidence of Pneumonia

Herd A – 265 head

<table>
<thead>
<tr>
<th></th>
<th>Pneumonic</th>
<th>Nonpneumonic</th>
<th>Percent</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Responders</td>
<td>2</td>
<td>34</td>
<td>5.6%</td>
<td></td>
</tr>
<tr>
<td>Vs. Herdmates</td>
<td>35</td>
<td>194</td>
<td>15.3%</td>
<td>p = 0.09</td>
</tr>
</tbody>
</table>

Herd B – 1267 head

<table>
<thead>
<tr>
<th></th>
<th>Pneumonic</th>
<th>Nonpneumonic</th>
<th>Percent</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Responders</td>
<td>11</td>
<td>149</td>
<td>6.9%</td>
<td></td>
</tr>
<tr>
<td>Vs. Herdmates</td>
<td>101</td>
<td>1006</td>
<td>9.1%</td>
<td>p = 0.22</td>
</tr>
</tbody>
</table>

Herd C – 2724 head

<table>
<thead>
<tr>
<th></th>
<th>Pneumonic</th>
<th>Nonpneumonic</th>
<th>Percent</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Responders</td>
<td>45</td>
<td>186</td>
<td>19.5%</td>
<td></td>
</tr>
<tr>
<td>Vs. Herdmates</td>
<td>683</td>
<td>1810</td>
<td>27.4%</td>
<td>p = 0.005</td>
</tr>
</tbody>
</table>
Better response to commercial vaccines

LsMEANS OF SERUM ANTIBODY TO J5 *E. coli* VACCINE

Reference: Wagter & Mallard et al 2000 JDS 83:488
Benefit # 3 - Better Quality Colostrum

Specific Antibody

Also:
Total IgG
B-Lactoglobulin

Ref - Wagter & Mallard et al JDS 83:488, 2000;
Fleming MSc Thesis, 2014
Benefit # 5 – Better Growth of Heifers

Average daily weight gains for immune response groups

Kg/day

ADG

AMIR
CMIR
CIR

* H L

100 Australian Heifer

REFERENCE - IMMUNE FUNCTION AS A PREDICTOR OF DAIRY CATTLE HEALTH AND DISEASE
J.W. Aleri, B.C. Hine, M.F. Pyman, P.D. Mansell, W.J. Wales, B.A. Mallard and A.D. Fisher
Benefit # 6 – Improvement in Lameness

- **High AMIR** cows had less Infectious Digital Dermatitis, but more Non-Infectious Hoof Lesions
- **High CMIR** cows tended to have less Interdigital hyperplasia

Leading Cause of Culling
Infectious Digital Dermatitis

- High 23%
- Ave 60%
- Low 50%

N=190

2014 Data from Mallard Group
Semex Approach

- Test all marketable proven bulls & the latest genomic bulls
- >1500 HO bulls tested, all Semex bulls are tested
- Top 10% for overall immune response qualify for Immunity+
No adverse reactions or CFIA cross-reactivity were found before and after HIR testing.
Bulls Designated as Immunity+

Approximately 10% of sires
### Disease Occurrence of Immunity+ Daughters

#### US Herd Milking 1500 Cows in 2013

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cattle</th>
<th>Immunity+ Daughters</th>
<th>All Other Daughters</th>
<th>Disease Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mastitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1\textsuperscript{st} lactation</td>
<td>8.8%</td>
<td>15.8%</td>
<td></td>
<td>44.3%</td>
</tr>
<tr>
<td><strong>All Recorded Disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1\textsuperscript{st} lactation</td>
<td>16.7%</td>
<td>18.2%</td>
<td></td>
<td>8.5%</td>
</tr>
<tr>
<td><strong>Pneumonia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heifers</td>
<td>6.8%</td>
<td>9.1%</td>
<td></td>
<td>25.3%</td>
</tr>
</tbody>
</table>

Disease reduction calculated as: (Disease incidence in all other daughters - disease incidence Immunity+ daughters) / Disease incidence in all other daughters * 100%

(Data Courtesy of Jay Shannon, Semex Alliance)
<table>
<thead>
<tr>
<th>By SID</th>
<th>Name</th>
<th># Heifers</th>
<th>PNEUM Rate</th>
<th>Scours Rate</th>
<th>PinkEye Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>200H5755</td>
<td>Alltop</td>
<td>336</td>
<td>10</td>
<td>3.0%</td>
<td>38</td>
</tr>
<tr>
<td>200H5565</td>
<td>Longtime</td>
<td>324</td>
<td>16</td>
<td>4.9%</td>
<td>33</td>
</tr>
<tr>
<td>200H5611</td>
<td>Sailing</td>
<td>301</td>
<td>5</td>
<td>1.7%</td>
<td>37</td>
</tr>
<tr>
<td>200H3559</td>
<td>Sleeman</td>
<td>625</td>
<td>7</td>
<td>1.1%</td>
<td>37</td>
</tr>
<tr>
<td>Herd</td>
<td>All Sires</td>
<td>18730</td>
<td>268</td>
<td>1.4%</td>
<td>2543</td>
</tr>
</tbody>
</table>

* Slide courtesy of Dany Peirre Rondeau – Sales Manager: Middle East, North Africa, Pakistan & Vietnam
Compared to all other Sires Tested for Immune Response using the HIR Method

<table>
<thead>
<tr>
<th>Trait of Interest</th>
<th>Average Proof for Immunity+ Sires</th>
<th>Difference between Immunity+ &amp; all other Sires Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>TPI</td>
<td>+ 2305</td>
<td>+186 Favorable</td>
</tr>
<tr>
<td>Net Merit</td>
<td>+$708</td>
<td>+$165 Favorable</td>
</tr>
<tr>
<td>Productive Life</td>
<td>+4.7</td>
<td>+1.6 Favorable</td>
</tr>
<tr>
<td>Daughter Preg Rate</td>
<td>+0.8</td>
<td>+0.70 Favorable</td>
</tr>
<tr>
<td>Somatic Cell Score</td>
<td>2.69</td>
<td>-0.11 Favorable</td>
</tr>
<tr>
<td>Daughter Calving Ease</td>
<td>5.7</td>
<td>-0.70 Favorable</td>
</tr>
</tbody>
</table>

(Data Courtesy of Jay Shannon, Semex Alliance)
Building a Stronger Herd

DAUGHTERS OF IMMUNITY+™ SIRES ARE EXPECTED TO HAVE

4 to 8% less disease

$80 per daughter added profit

Including mastitis, metritis, ketosis and retained placenta. Early indications show a desired response to Johnes as well.

In addition to the $ value of the genetics for other traits.

Dr Chesnais, Senior Geneticist, Semex
Our Current Research on Genomics of Immune Response
The Power of Genomics
Genetic Gain in Dairy Cattle

Figure 1: Genetic Trend of Young Holstein Bulls Released in Canada for Lifetime Profit Index (GLPI)

- Average Gain: 445 LPI points/year
- Average Gain: 210 LPI points/year
- Average Gain: 109 LPI points/year

Period of Semen Release in Canada
(Group 1=Jan-Jun, Group 2=Jul-Dec within Year)

Official adoption of Genomics 2008

B. Van Doormaal, Canadian Dairy Network, July 2012,
Increased Rates of Genetic Gain with Genomics
GWAS was performed on Holsteins (n=680 cows, 543 bulls) classified on IR and **selective genotyping** of **High** or **Low** responder using the SNP50

**Lo - Cows**
- 82 = L-AMIR
- 65 = L-CMIR

**Un-related Bulls**
- 81 = L-AMIR
- 72 = L-CMIR

**Hi - Cows**
- 81 = H-AMIR
- 75 = H-CMIR

**Un-related Bulls**
- 83 = H-AMIR
- 74 = H-CMIR

2,580 SNP significantly \((P < 0.05)\) associated with AMIR

Result: 186 SNP following 5% correction for false discovery rate

2,791 SNP significantly \((P < 0.05)\) associated with CMIR

Result: 21 SNP following 5% correction for false discovery rate

Establish a large reference population of 5000 cows and >2000 Semex bulls within Canada

- Western Provinces: 500 cows
- Ontario: 2000 cows
- Quebec: 2000 cows
- Atlantic Provinces: 500 cows
Knowledge of **HIR gene profiles** should enhance selection for **disease resistance**

Allow **broader application** of the HIR technology by inclusion IR traits in genomic evaluations
Genetic Selection for Immune Response can Improve Dairy Health Management -

- Via Improved Breeding & Culling Decisions
- Via Improved Vaccine Protocols
- Via Improved Colostrum Management
- Via Improving other Fitness Traits
Our Current Research also shows Epigenetic Influences on the Bovine Immune System

Ref – Hussey, Paibomesai and Mallard, CJVR 77:54, 2013
TAKE HOME - What you do today can effect the generations of tomorrow

- Genetics
- Epigenetics
- Environment

- Phenotype
Funding is gratefully acknowledged from:
NSERC
OMAFRA
CDN
Dairy Gen
Semex Alliance