Genome-wide association study and functional analysis of infectious and horn type hoof lesions in Canadian Holstein cattle

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Lameness considered the number one health issue by Canadian dairy producers

Prevalence of 30 to 70% of cows with at least one hoof lesion – North America and Europe
Classification of Hoof Lesions

- Hoof lesions traditionally classified according to their etiology and pathogenesis:
  - **Infectious or partly infectious lesions:** Mostly related to environmental hygiene
    - e.g., Digital and interdigital dermatitis, foot rot, and heel erosion
  - **Horn lesions:** Mostly caused by metabolic or mechanical factors
    - e.g., Sole and toe ulcer, sole hemorrhage, and white line disease
Weak genetic correlations reported between infectious and horn lesions

Defining candidate genes harboring important regions will allow a more comprehensive understanding of the mechanisms involved in these different groups of lesions

- Potentially contribute to a more accurate genetic selection for these traits
Objective

- To perform a genome-wide association study and a functional analysis for infectious and horn lesions in Canadian Holstein cattle
Data

- 249,709 records from 105,450 cows
- 1,080 Canadian herds between 2009 and 2016
- 51 hoof trimmers
- Hoof supervisor® system (KS Dairy Consulting, Dresser, Wisconsin)
- Pedigree file 331,587 animals
Lesions classified according to their etiology and pathogenesis

- **Infectious/partly infectious lesions**: digital and interdigital dermatitis, foot rot, and heel erosion
- **Horn lesions**: sole and toe ulcer, sole haemorrhage, and white line disease

Hoof lesions considered as binary variables

- 0: no lesion
- 1: presence of a lesion
• Linear animal model DMU (Madsen and Jensen, 2008):

\[ Y = \mu + \text{HERD} + \text{TRIMMER} + \text{PARITY} + \text{STAGE} + a + pe + e \]

HERD: herd-date of hoof trimming
TRIMMER: hoof trimmer
PARITY: parity at trimming
STAGE: stage of lactation at trimming
a: random additive genetic animal effect
pe: random permanent environmental effect
e: random error term
De-regressed EBV \cite{VanRaden2009}

EBV reliability greater than 0.10 and genotyped
- 13,657 for Horn Lesions
- 13,834 for Infectious Lesions

Animals genotyped (or imputed) 50K
• Direct genomic values for each animal and trait predicted based on the GBLUP method (VanRaden, 2008)
  – De-regressed EBV as pseudo-phenotypes
• SNP effects obtained using POSTGSF90
• 20-adjacent-SNP moving windows explaining more than 0.30% of genetic variance
Infectious and Horn Lesions - Prevalence

- Infectious Lesions: 21%
- Horn Lesions: 18%

[Chart showing prevalence of infectious and horn lesions]
Infectious Lesions
Infectious Lesions

**BTA10 (0.47%):**
- **AHSA1, PELI2**
- Associated with response to stress and immune system processes
BTA 2,3,14:
- **ZAK, CDCA7, CD1E**
- Associated with embryonic digit morphogenesis, regulation of cell proliferation and apoptotic processes, antigen processing and presentation
Horn Lesions
Horn Lesions

**BTA5 (1.23%)**:
- **STYK1, TULP3**
- Associated with innate immune response, cartilage development and embryonic digit morphogenesis
Horn Lesions

BTA5 (1.23%):
• *STYK1, TULP3*
• Associated with innate immune response, cartilage development and embryonic digit morphogenesis

BTA6 (0.83%):
• *BDH2*
• Associated with collagen metabolic process
Horn Lesions

BTA25 (0.66%):

• **PLOD3, SH2B2**
• Associated with epidermis morphogenesis, collagen fibril organization, collagen metabolic process regulation of immune response
Horn Lesions

BTA1, BTA9, BTA15, BTA16, BTA20, BTA21, BTA25, BTA28
(>0.30%)
• Important genomic regions associated with infectious and horn lesions were identified
• List of functional candidate genes within or next to these regions was created
• The next step is to perform analyses for individual hoof health traits
Supported by a contribution from the Dairy Research Cluster Initiative (Dairy Farmers of Canada, Agriculture and Agri-Food Canada, the Canadian Dairy Network and the Canadian Dairy Commission), Alberta Milk, and by Ontario Genomics
# Genetic correlations between hoof lesions

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<tr>
<th>Traits</th>
<th>ID</th>
<th>IH</th>
<th>SH</th>
<th>SU</th>
<th>TU</th>
<th>White Line</th>
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<tbody>
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<td>Digital Dermatitis (DD)</td>
<td>0.54</td>
<td>0.60</td>
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<td>Interdigital Dermatitis (ID)</td>
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<td>Sole Hemorrhage (SH)</td>
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<td>Sole Ulcer (SU)</td>
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<td>Toe Ulcer (TU)</td>
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