Underlying genetic architecture of mastitis: A systematic review, meta and gene prioritization analysis of GWAS results

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Background

- Mastitis is a complex polygenic disease that is regulated by several genes with small effects.
- We performed a systematic review, meta- and gene prioritization analysis of genome-wide association study (GWAS) studies to identify key genetic markers and genes associated with mastitis-related traits and somatic cell score (SCS) in dairy cattle.

Materials and Methods

- Systematic review question followed the PPQ framework (population: dairy cattle; prognostic tool: GWAS; outcome: mastitis and SCS).
- Search was conducted using electronic databases, conference proceedings and industry meeting reports.
- Gene prioritization analysis: GUIDify and ToppGene.
- Meta-analysis: Han and Eskin's random effects model in METASOFT.

Preliminary results

- Imported studies (n = 3,936)
  - Removed duplicates (n = 1,925)
- Screened abstracts (n = 2,011)
  - Irrelevant studies (n = 1,357)
- Screened full-texts (n = 654)
  - Excluded studies (n = 566)
    - Duplicate (n = 11)
    - Not original study (n = 8)
    - Wrong population (n = 3)
    - Not GWAS (n = 506)
    - Wrong outcome (n = 32)
    - No abstract available (n = 6)
- Reference and citation checking (n = 1)
  - Not yet analyzed (n = 75)
    - Full-text requested (n = 44)
    - Breed was not Holstein (n = 8)
    - Outcome not mastitis (n = 23)
- Included studies (n = 89)
  - Preliminary analysis (n = 14)

Table 1: Characteristics of included 14 studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of genotyped animals</th>
<th># SNPs used for the analysis</th>
<th># variants associated with mastitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cai 2018</td>
<td>5,147 bulls</td>
<td>15,552,968</td>
<td>22 SNPs</td>
</tr>
<tr>
<td>Fang 2017a</td>
<td>5,056 cattle</td>
<td>15,355,382</td>
<td>5 GO</td>
</tr>
<tr>
<td>Fang 2017b</td>
<td>5,056 cattle</td>
<td>15,355,382</td>
<td>5 SNPs</td>
</tr>
<tr>
<td>Fang 2018</td>
<td>5,056 cattle</td>
<td>15,355,382</td>
<td>5 QTL</td>
</tr>
<tr>
<td>Kurz 2019</td>
<td>43 cows</td>
<td>585,949</td>
<td>116 SNPs, 27 QTLs</td>
</tr>
<tr>
<td>Ma 2019</td>
<td>3,114 bulls</td>
<td>15,388,916</td>
<td>405 markers</td>
</tr>
<tr>
<td>Marete 2018a</td>
<td>46,732 cattle</td>
<td>40,810</td>
<td>11 SNPs</td>
</tr>
<tr>
<td>Marete 2018b</td>
<td>32,491 cows</td>
<td>49,835</td>
<td>28 SNPs</td>
</tr>
<tr>
<td>Naderi 2018</td>
<td>6,744 cows</td>
<td>43,939</td>
<td>4 SNPs</td>
</tr>
<tr>
<td>Sahana 2013</td>
<td>5,035 bulls</td>
<td>648,219</td>
<td>23 SNPs</td>
</tr>
<tr>
<td>Sahana 2014</td>
<td>2,098 bulls</td>
<td>36,387</td>
<td>143 SNPs</td>
</tr>
<tr>
<td>Su 2014</td>
<td>5,643 bulls</td>
<td>44,919</td>
<td></td>
</tr>
<tr>
<td>Tiezzi 2015</td>
<td>1,361 bulls</td>
<td>39,004</td>
<td>10 SNP windows</td>
</tr>
<tr>
<td>Yang 2019</td>
<td>40 cows</td>
<td>10,058</td>
<td>27 SNPs</td>
</tr>
</tbody>
</table>

- A clear definition of mastitis was absent in most of the studies.
- Cases in either the first, second or third lactation were often considered within studies.
- Quality assessment predominately focused on the handling of genomic data and the selection of SNPs for the GWAS.
- Various methods were used to conduct the GWAS.
- Reported outcomes varied across 14 studies.
- Identified genes were mostly associated with immune-related processes.

Figure 1: PRISMA flow diagram

Figure 2: Origin of data (A) and lactation considered (B), 14 studies

Figure 4: Commonly reported genes among the 14 pre-analysed studies

Conclusion

- 89 articles were identified.
- Among 14 studies immune-related 6 common genes were identified.

Significance

This systematic review will add value in summarizing GWAS findings to better understand the genetic architecture of mastitis in dairy cattle.