Genome-wide association identify regions underlying bovine tuberculosis resistance in dairy cattle

K. Raphaka¹, O. Matika¹, E. Sanchez-Molano¹, R. Mrode², M. Coffey², V. Riggio¹, E.J. Glass¹, J.A. Woolliams¹ and G. Banos¹,²

¹The Roslin Institute and Royal (Dick) School of Veterinary Studies, Edinburgh, UK
²Scotland’s Rural College, Edinburgh, UK

29 Aug – 2 Sept 2016
Belfast, UK
A chronic disease of cattle caused by *Mycobacterium bovis*

**Diagnosis of TB in UK:**

- **Skin test**
  - Positive animals are culled

- **Post-mortem examination**
  - Inspected for visible lesions
  - Bacteriological culture for *M. bovis*
Background

- Increasing bTB incidences in GB despite decades of control strategies

- Estimated expenditure for GB was £152 million in 2010/2011 (Abernethy et al. 2013)
Host genetic variance

- Genetic component to cattle resistance to bTB
  - Heritability = 0.11 – 0.23
- Selection for resistant animals feasible

![Diagram showing distribution of EBVs with categories: highly susceptible, less susceptible]
### Association studies for bTB resistance in cattle

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country</th>
<th>Cattle type</th>
<th>No. of obs.</th>
<th>Chromosome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finlay et al., 2012</td>
<td>ROI</td>
<td>Dairy</td>
<td>307</td>
<td>22</td>
</tr>
<tr>
<td>Bermingham et al., 2014</td>
<td>NI</td>
<td>Dairy</td>
<td>1151</td>
<td>2, 13</td>
</tr>
<tr>
<td>Richardson et al., 2016</td>
<td>ROI</td>
<td>Dairy</td>
<td>842</td>
<td>23</td>
</tr>
<tr>
<td>Tsairidou et al., 2014</td>
<td>ROI and NI</td>
<td>Dairy</td>
<td>1438</td>
<td>6</td>
</tr>
<tr>
<td>Kassahun et al., 2015</td>
<td>Ethiopia</td>
<td>Mixed breed pop.</td>
<td>585</td>
<td>6</td>
</tr>
</tbody>
</table>
Study objective

To identify genomic regions associated with bTB resistance in British dairy cattle using single SNP and regional heritability mapping analyses
Phenotypes

- dEBVs of 804 Holstein Friesian bulls and based on 3 trait definitions
  - skin test reactors with positive post-mortem/confirmed cases (RP)
  - skin test reactors regardless of post-mortem (R)
  - skin test reactors plus negative reactors with positive post-mortem results (RNP)

<table>
<thead>
<tr>
<th>Trait</th>
<th>N</th>
<th>Mean dEBVs</th>
<th>Mean reliability</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>RP</td>
<td>764</td>
<td>0.38</td>
<td>0.69</td>
<td>-7.72</td>
<td>7.84</td>
</tr>
<tr>
<td>R</td>
<td>784</td>
<td>0.44</td>
<td>0.74</td>
<td>-8.83</td>
<td>13.01</td>
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<tr>
<td>RNP</td>
<td>784</td>
<td>0.47</td>
<td>0.74</td>
<td>-9.02</td>
<td>13.50</td>
</tr>
</tbody>
</table>
Genotypes

- **56,134 SNPs**

- **Quality control**
  - MAF (0.02)
  - Ind. call rate (0.95)
  - SNP call rate (0.95)
  - HWE (1e-6)

- **Post QC**
  - 36,720 SNPs
  - No. of individuals: RP=759, R=779, RNP=779.
Suggestive SNPS on chromosomes 2 and 24
Single SNP association

- Suggestive SNP on chromosomes 23

\( h^2 = 0.37 \)
SNPs on chromosomes 23 below suggestive threshold but same SNPs as in RS
Regional heritability mapping (RHM)

- Suggestive regions identified
- Regional heritability range from 0.05 – 0.06
Regional heritability mapping (RHM)

- **Genome-wide significant regions**
- **Regional heritability range from 0.05 – 0.07**
Regional heritability mapping (RHM)

- Same regions as in R reach genome-wide threshold
- Regional heritability range from 0.06 – 0.08
Summary

- Lack of consistency in GWAS results
  - QTL regions identified differ from those previously reported
- GWAS and RHM analyses
  - Single SNP and RHM analyses found similar results
  - SNPs with moderate individual effects collectively have significant impact on bTB resistance
Summary

- **Potential for use in breeding**
  - Opportunity for exploration of candidate genes
  - Polygenic trait, genomic selection likely more effective than marker based selection

- **Future work**
  - Confirmation with independent data
  - Increase of power by including more observations
Acknowledgements

- S. Wilkinson (Roslin)
- L. Muhlbauer (Roslin)
- L. Seeker (SRUC)
- A. Psifidi (Roslin)
- J. Ilska-Warner (SRUC)
- T. Englishby (SRUC)
- T. Krzyzelewski (SRUC)
- A. Brown (SRUC)
- O. Abejide (SRUC)