



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

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Background



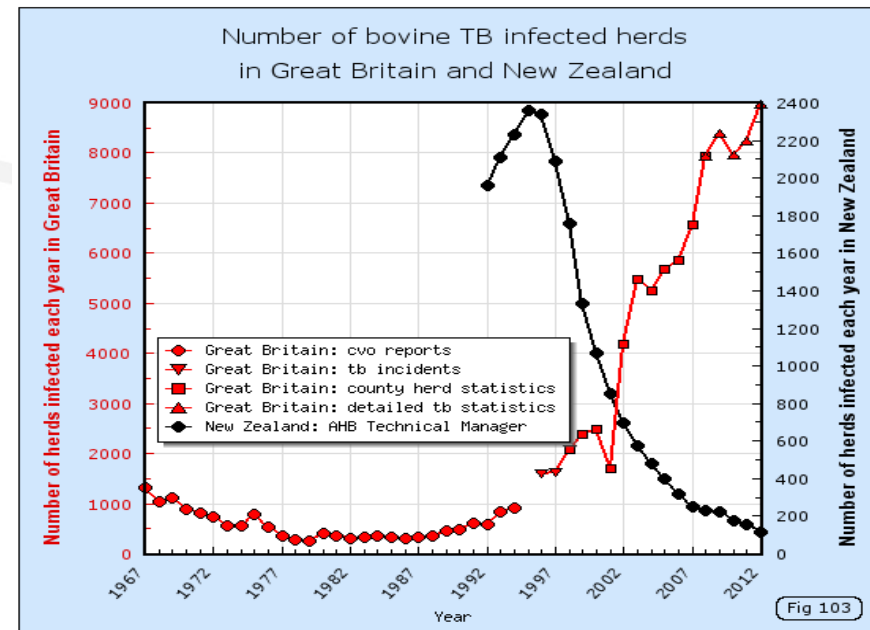
- ❑ A chronic disease of cattle caused by *Mycobacterium bovis*
- ❑ Diagnosis of TB in UK:
 - **Skin test**
 - Positive animals are culled
 - **Post-mortem examination**
 - Inspected for visible lesions
 - Bacteriological culture for *M. bovis*



Background



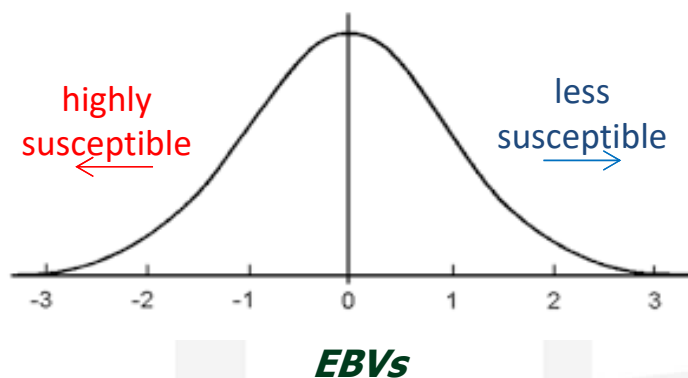
- Increasing bTB incidences in GB despite decades of control strategies
- Estimated expenditure for GB was £152 million in 2010/2011 (Abernethy *et al.* 2013)



Host genetic variance



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





Association studies for bTB resistance in cattle

Authors	Country	Cattle type	No. of obs.	Chromosome
Finlay et al., 2012	ROI	Dairy	307	22
Bermingham et al., 2014	NI	Dairy	1151	2, 13
Richardson et al., 2016	ROI	Dairy	842	23
Tsairidou et al., 2014	ROI and NI	Dairy	1438	6
Kassahun et al., 2015	Ethiopia	Mixed breed pop.	585	6

Study objective



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



- **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)**

Trait	N	Mean dEBVs	Mean reliability	Min.	Max.
RP	764	0.38	0.69	-7.72	7.84
R	784	0.44	0.74	-8.83	13.01
RNP	784	0.47	0.74	-9.02	13.50



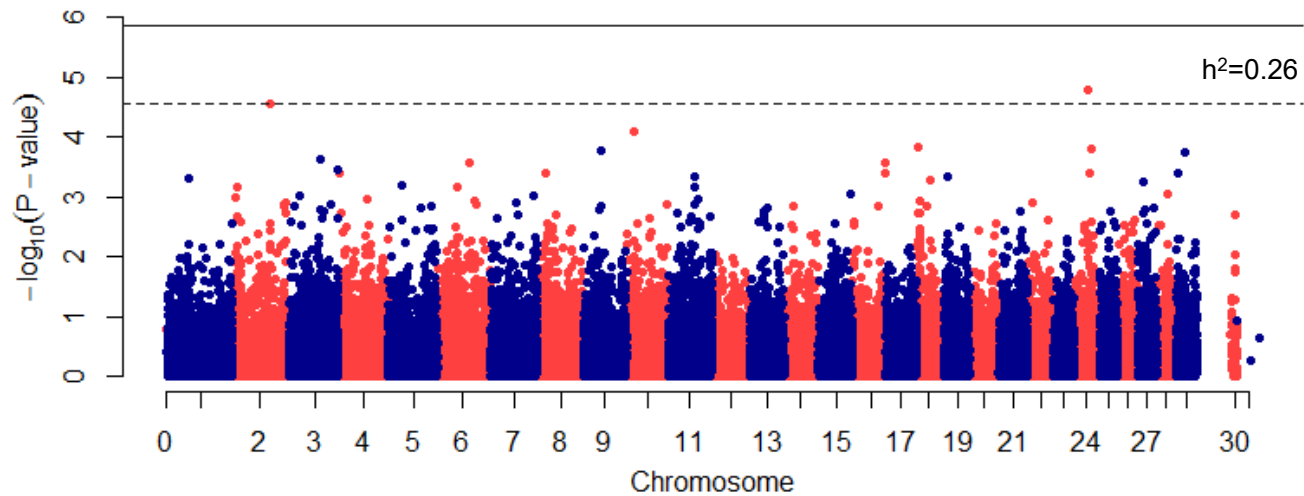
- **56,134 SNPs**
- **Quality control**
 - **MAF (0.02)**
 - **Ind. call rate (0.95)**
 - **SNP call rate (0.95)**
 - **HWE ($1e-6$)**
- **Post QC**
 - **36,720 SNPs**
 - **No. of individuals: RP=759, R=779, RNP=779.**



Single SNP association



RP



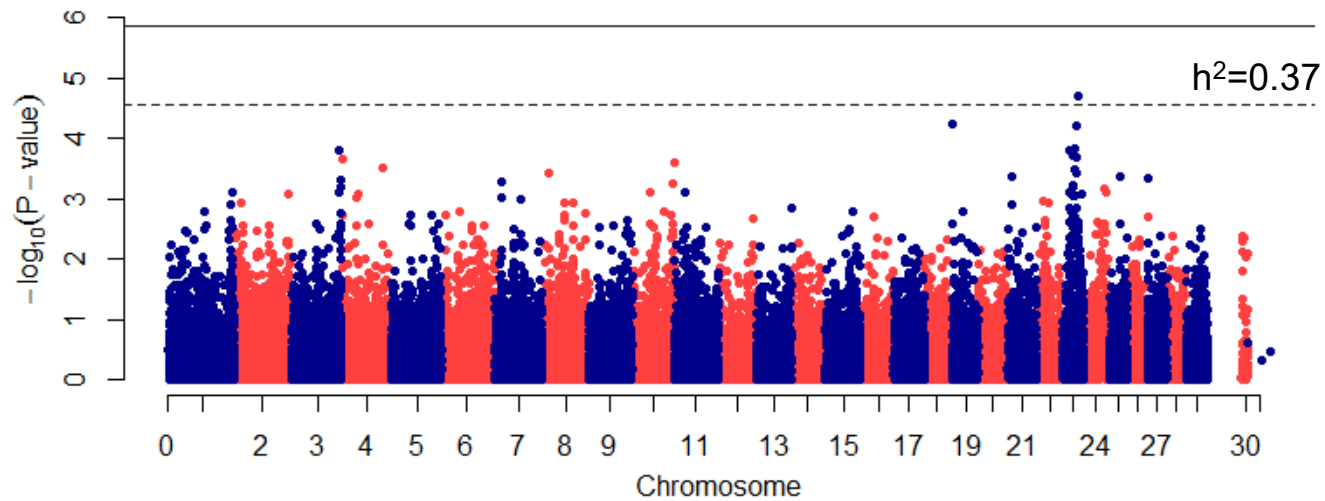
■ Suggestive SNPS on chromosomes 2 and 24



Single SNP association



□ R



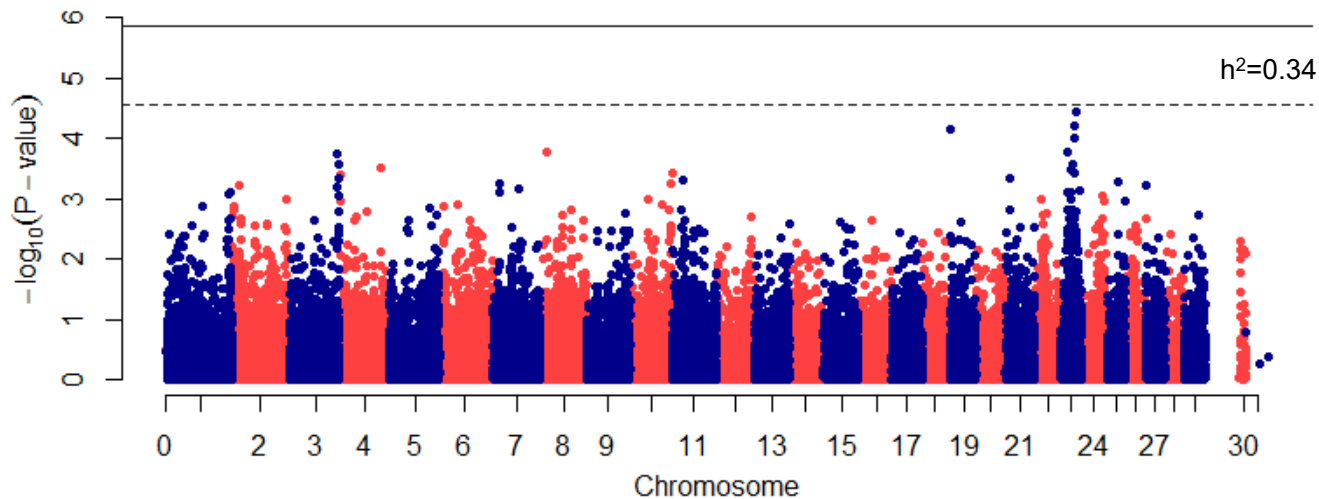
- Suggestive SNP on chromosomes 23



Single SNP association



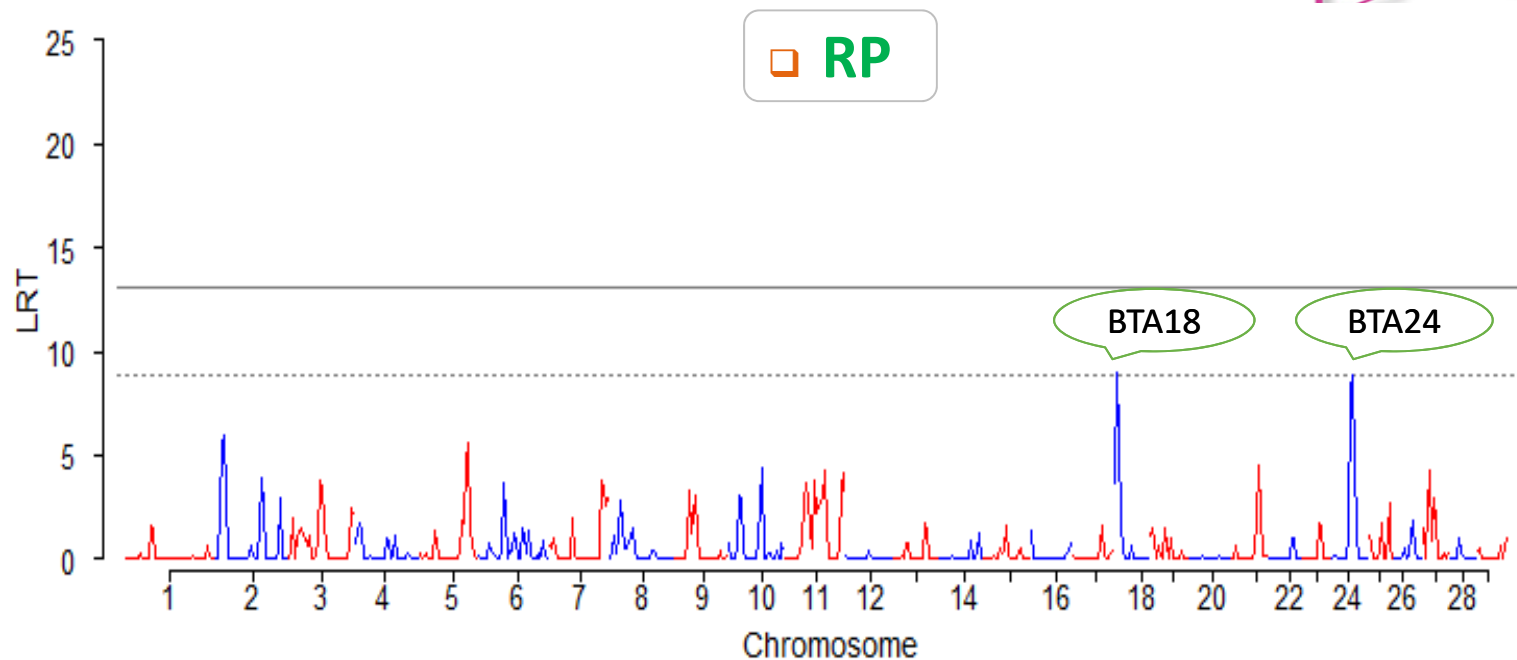
RNP



- SNPs on chromosomes 23 below suggestive threshold but same SNPs as in RS



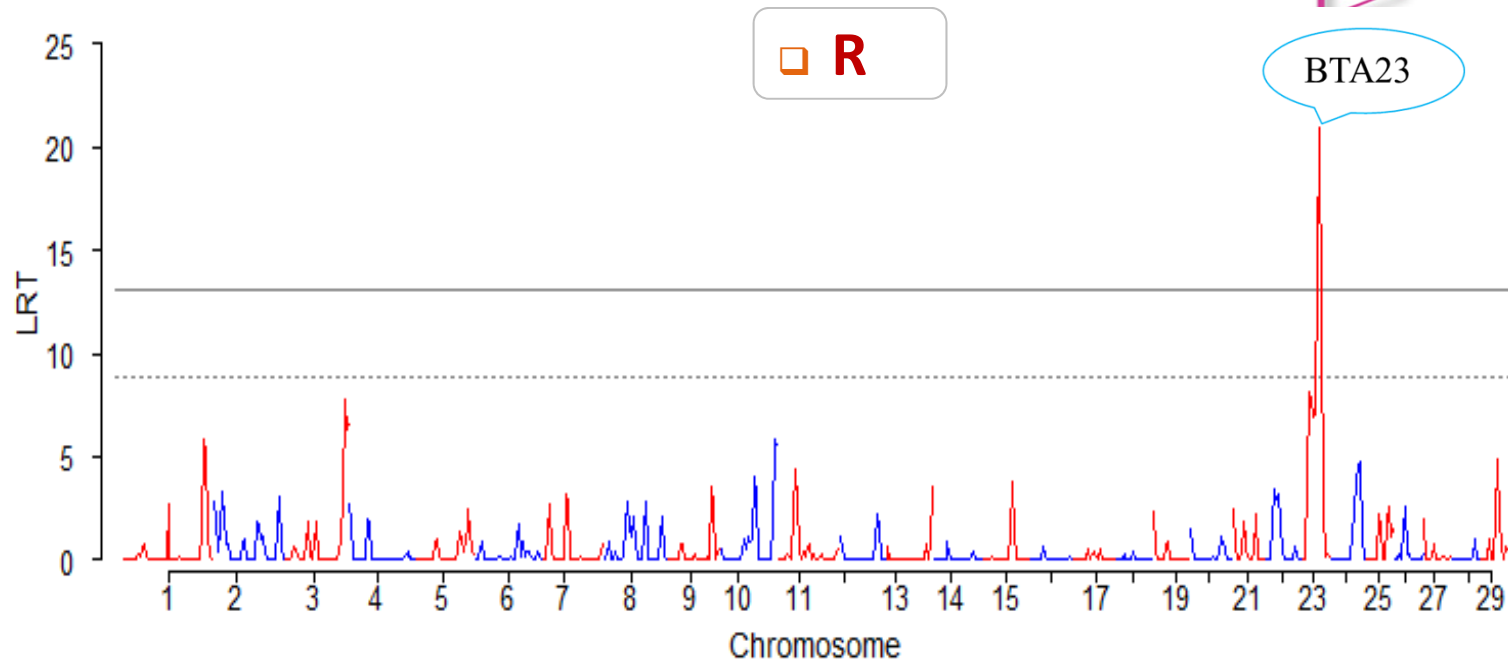
Regional heritability mapping (RHM)



- Suggestive regions identified
- Regional heritability range from 0.05 – 0.06



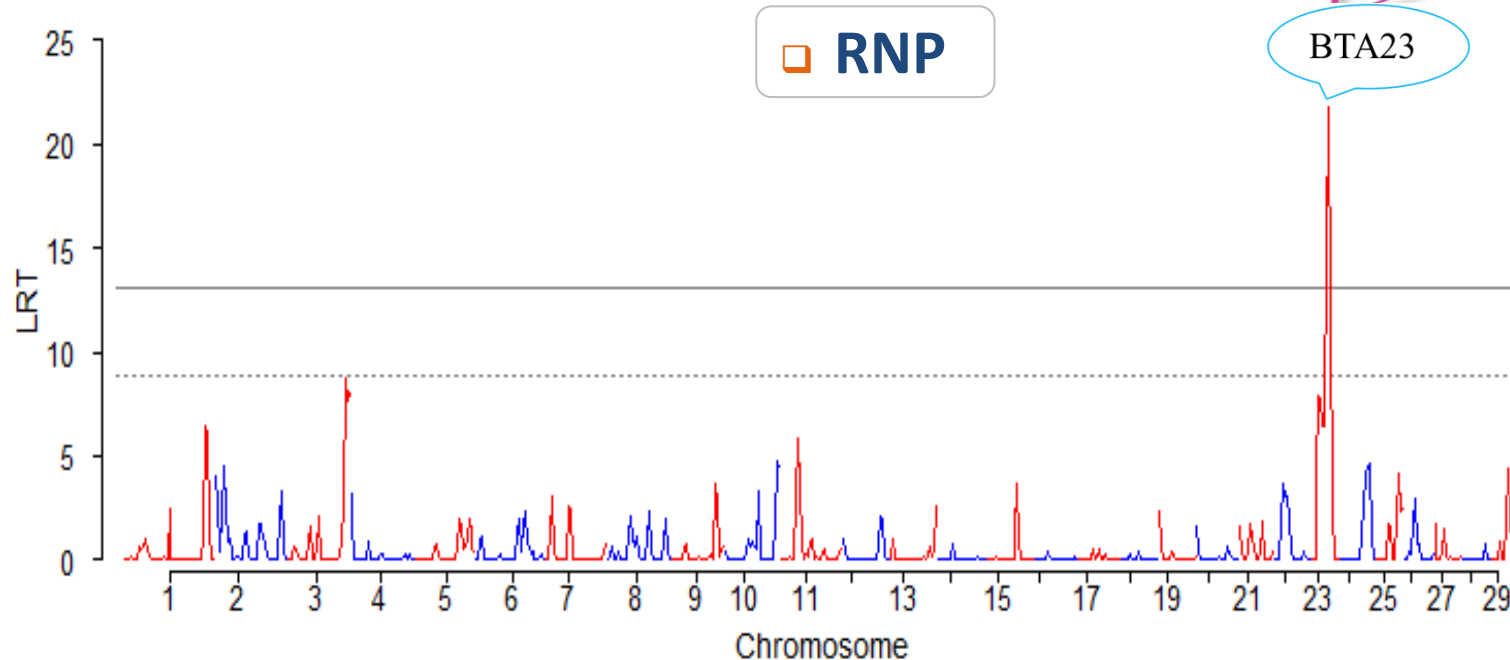
Regional heritability mapping (RHM)



- **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



- **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**



- **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**



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