

# Genome-wide association for facial eczema tolerance in New Zealand sheep

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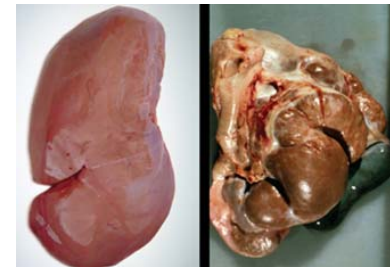
# Facial Eczema (FE)

Long-running animal health challenge of the upper part of New Zealand

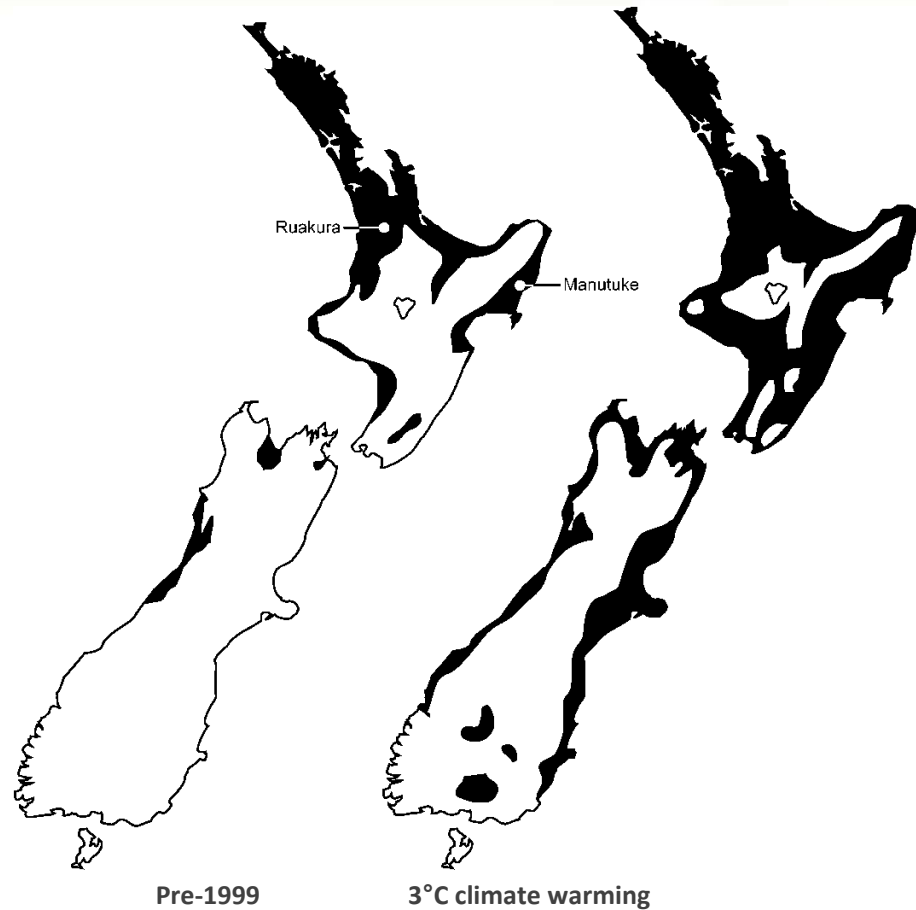
Metabolic disease caused by toxic spores of the fungus *Pithomyces chartarum*

- Results in liver and bile duct damage
- Sub-clinical FE = Liver damage
- Clinical FE = Photosensitivity

Both clinical & sub-clinical FE → decreased production & reproduction



# Geographic Spread of Facial Eczema



# Controlling Facial Eczema

Preventative treatment with zinc

Tolerance to FE is a heritable trait in sheep ( $h^2 = 0.44$ )<sup>1</sup>

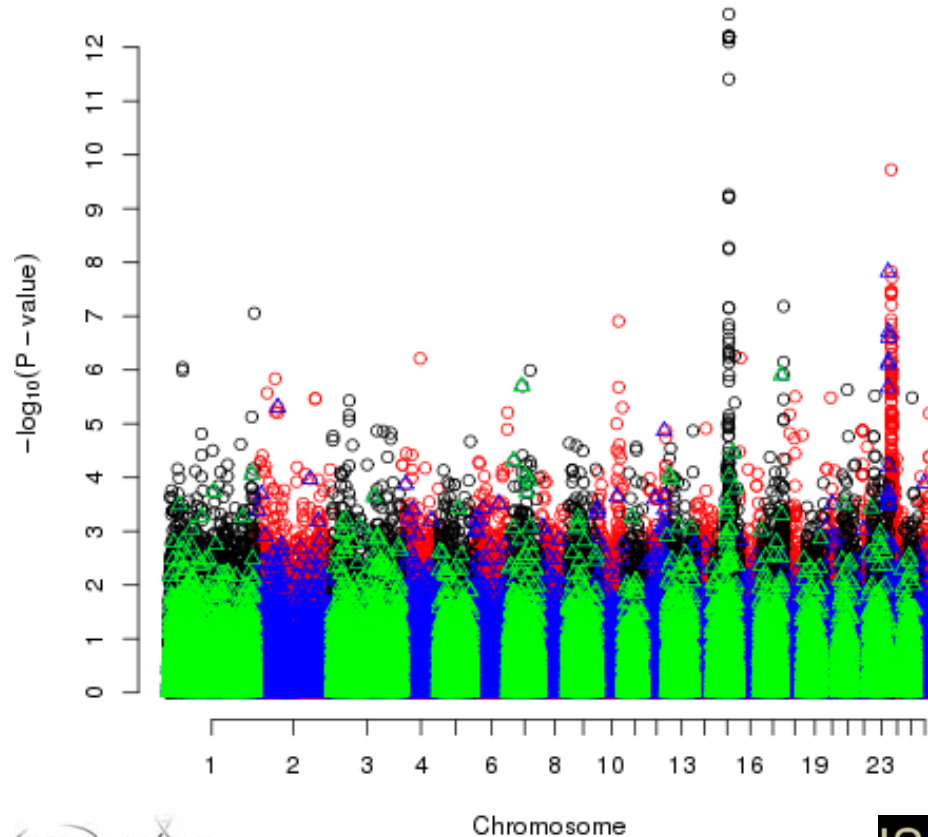
- Measured sporidesmin challenge, measure liver damage 21 days afterwards (GGT21)
- Generate breeding values

A commercial testing program, Ramguard, was set up in the 1980's to provide this service

- Dosing 800-1,000 rams each year



# Original GWAS



Single SNP association tests

- GRAMMAR analysis in GenABEL
- Imputed genotype data (50K & HD)
- 3,763 animals with FE phenotypes

→ SNP in significant regions on 15K chip

# Animal selection

## Utilised the RamGuard dataset<sup>1</sup>

- GGT levels 21 days after a measured sporidesmin challenge (GGT21)
- Flocks needed  $\geq 45$  animals with recorded GGT21
- Contemporary group  $\geq 4$  animals, and  $\geq 30\%$  animals with elevated GGT21 ( $> 70$ )

## Animals selected based on genotype availability

- Illumina OvineLD BeadChip (15,000 markers)

1,931 animals from 39 flocks, born between 2010 and 2014

# Association analyses

## 1) Efficient Mixed-Model Association eXpedited (EMMAX) analysis

- Phenotypic data (GGT21)
- Fitting contemporary group (flock.year.sex.GGT21mob)
- Identity-by-state (IBS) and first two principal components fitted

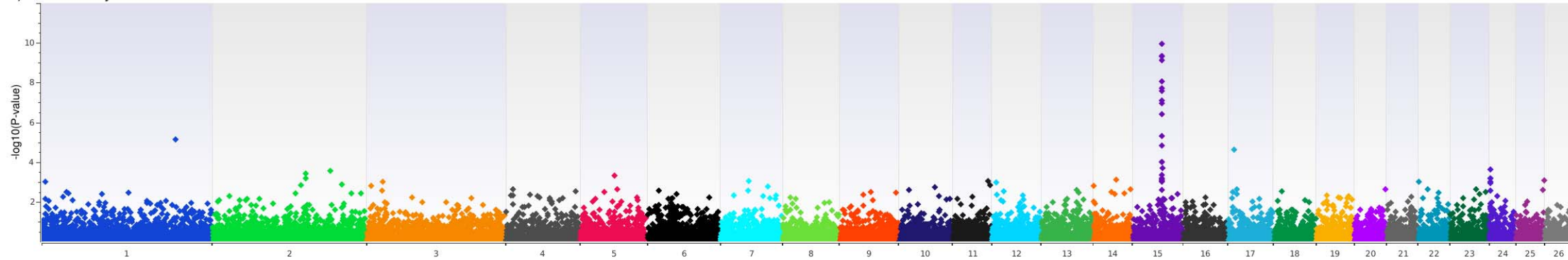
## 2) Genotype association test

- Residuals obtained from ASReml (fitting contemporary group)
- first two principal components fitted

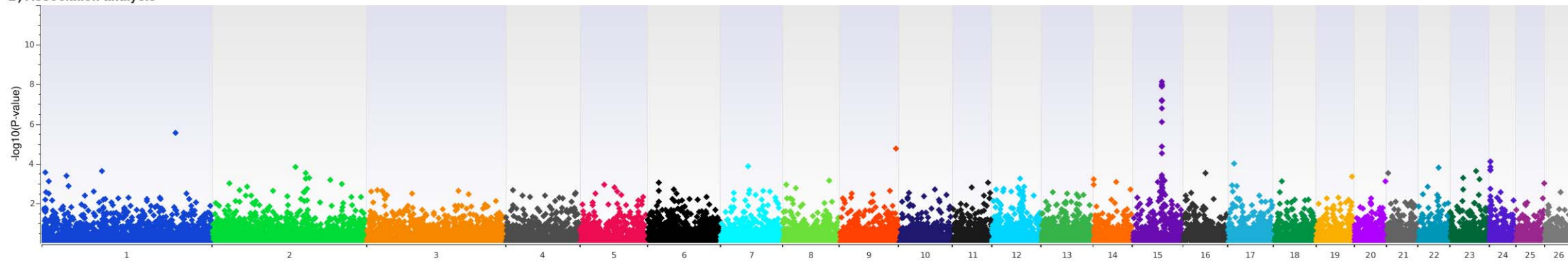
SNP effects fitted in ASReml

# Association analyses

A) EMMAX analysis

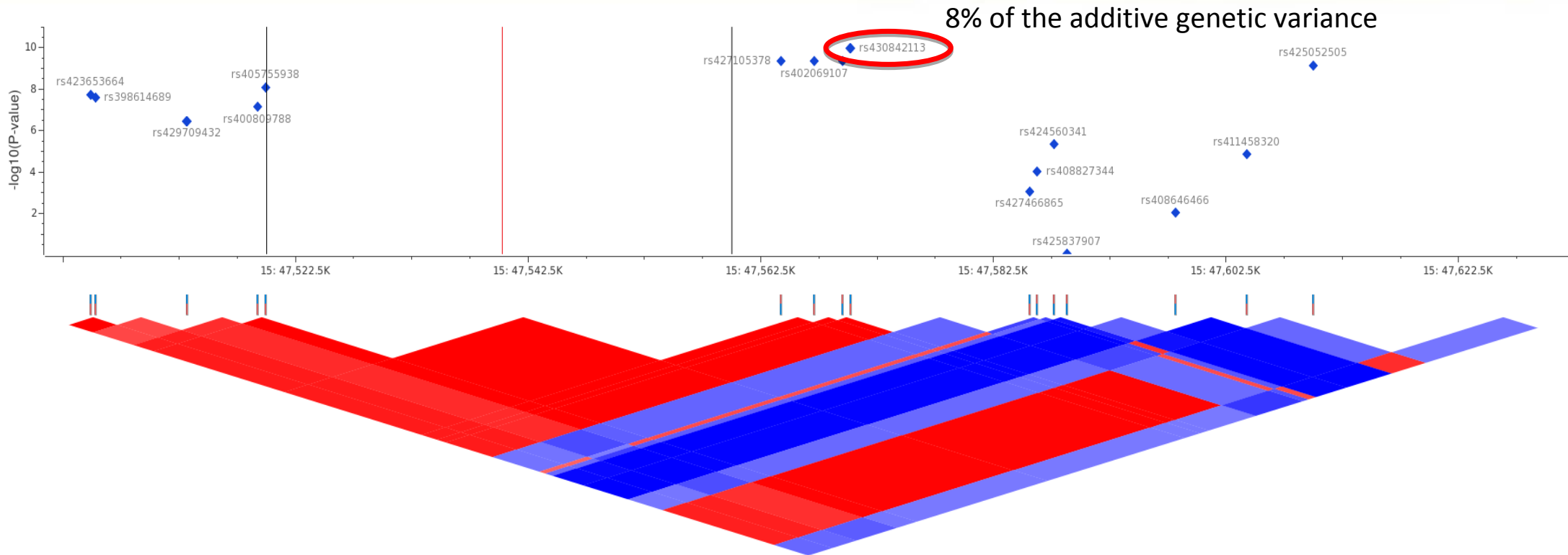


B) Association analysis

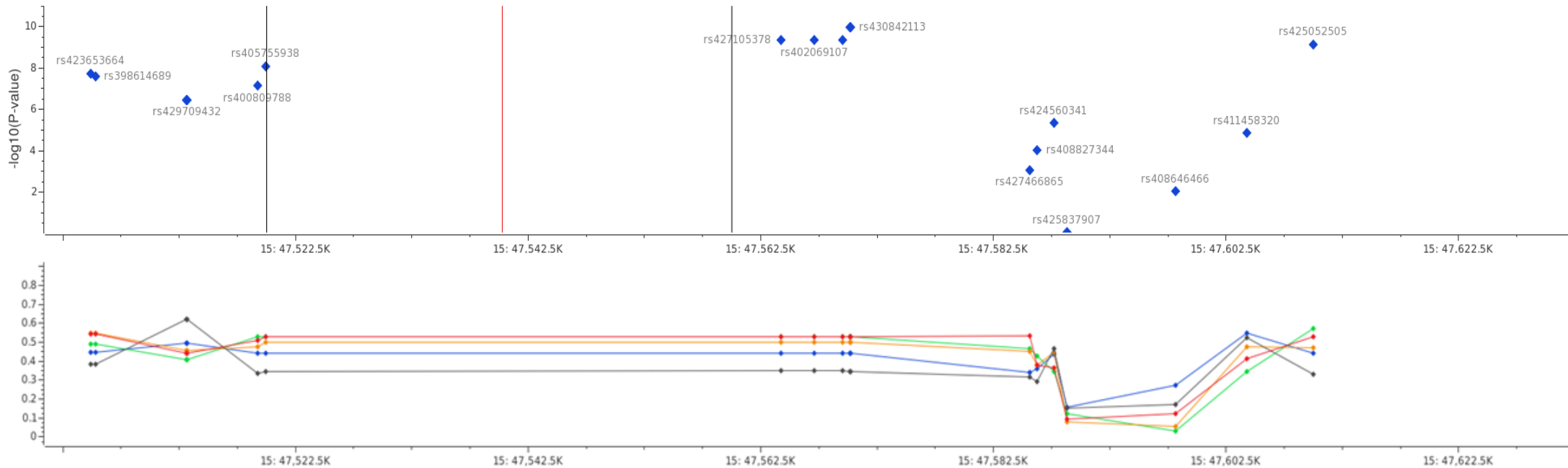




# Chromosome 15

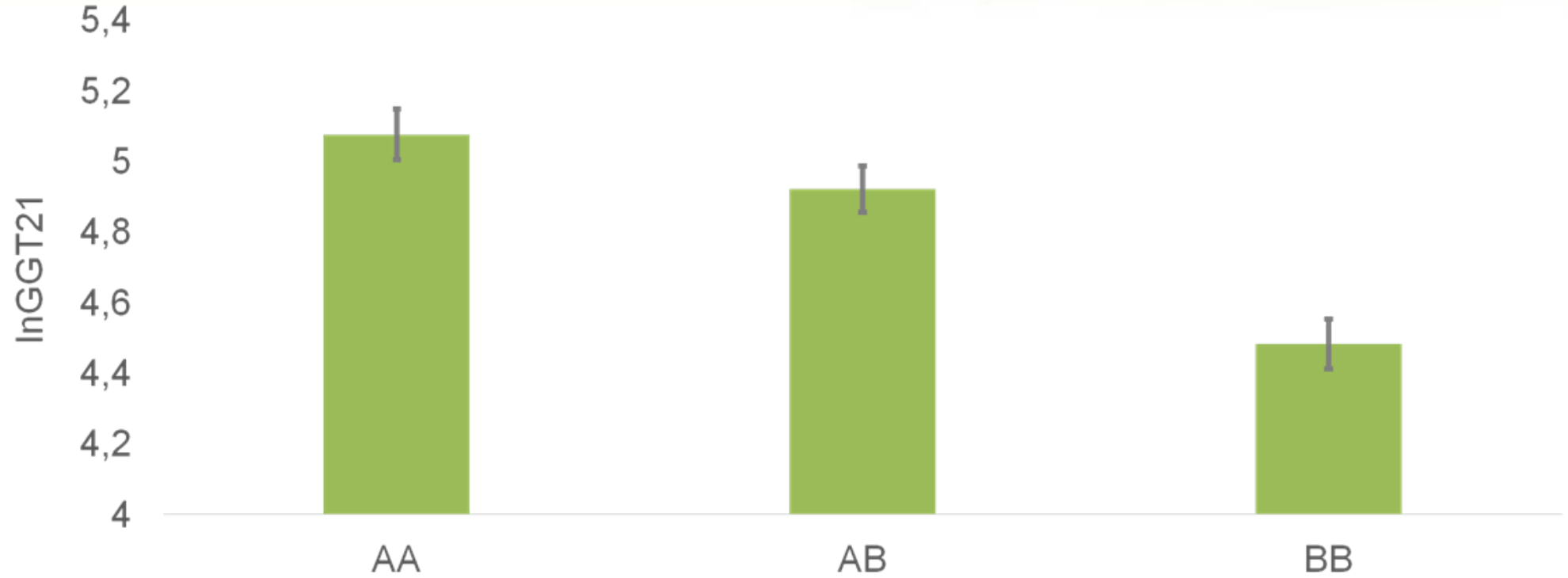


# Chromosome 15



Coopworth ◆; Highlander ◆; Perendale ◆; Composite ◆; Romney ◆

# Top SNP



# Beta - globin locus



~37 Kb insertion



OARv3.1



# Ovine beta globin

HapA and HapB both contain the ovine  $\beta^A$  gene (*HBB*)

- Differ by at least 7aa → considered allelic variants
- Haemoglobin from HapA (Hb-A) and HapB (Hb-B) sheep is distinguishable electrophoretically

HapA has been associated with:

- ↓ mastitis and ↑ parasite resistance in crossbred ewes<sup>1</sup>
- Resistance to photosensitisation (alveld) as a result of ingestion of *Nathercium ossifragum*<sup>2</sup>

# Haemoglobin and FE

SNP on either side of locus are in LD

- May be predictive of haemoglobin haplotype
- Needs to be validated

Potential role of haemoglobin type in the response to FE

- Not straightforward
- Toxicity of sporidesmin believed to be through the generation of superoxide radicals
- Conflicting evidence links between haemoglobin type and antioxidant enzymes

# Summary

Validation of previous QTL, discovered using HD genotypes

Peak on chromosome 15 at the  $\beta$ -globin locus

- Explains 8% of the additive genetic variance
- Haemoglobin haplotypes have previously been associated with variation in a number of health related traits in sheep
- Warrant more investigation into their role in tolerance to FE

# Acknowledgements

