Genetic architecture of resistance to virulent footrot in New Zealand Merino

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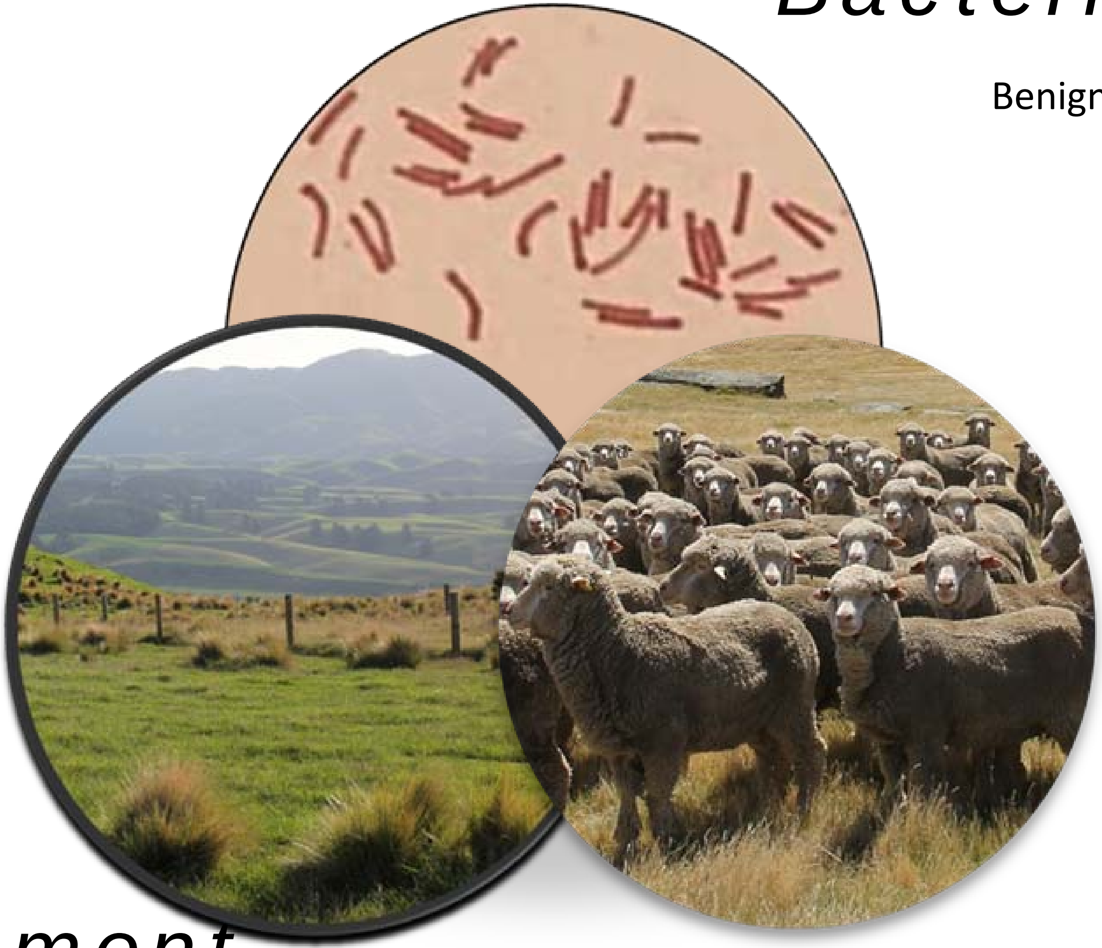
Multi-factorial disease



Bacteria

Benign **VIRULENCE** Virulent

19 serogroups & sub-types
A,B,C,D,E,F,G,H,I,M

Host

Res **SUSCEPTIBILITY** Sus

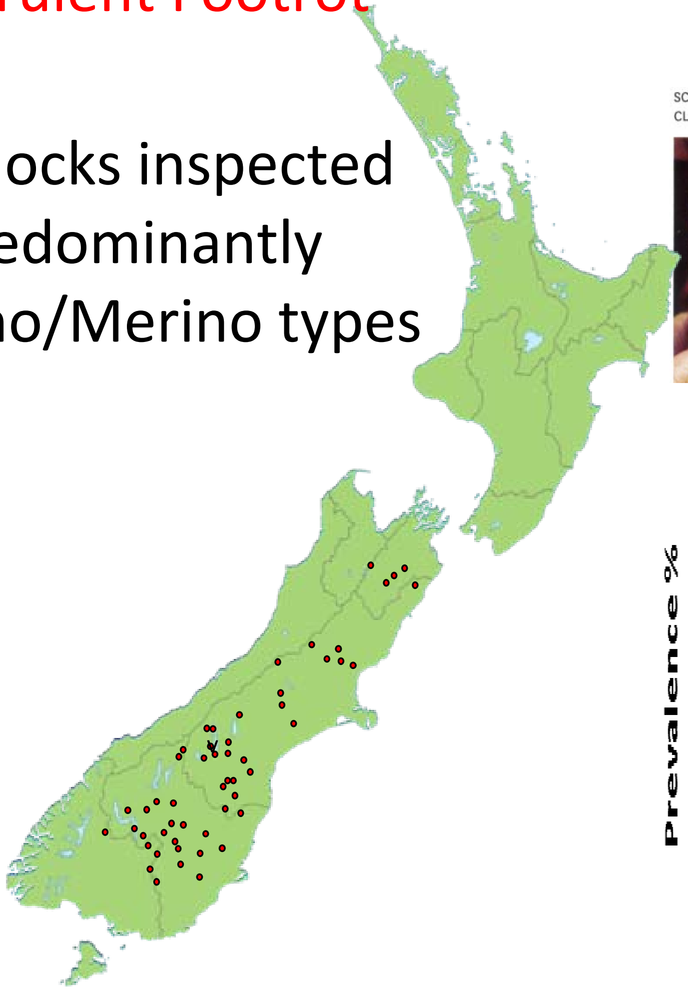
Management –limited & short term
Genetic variation

Environment

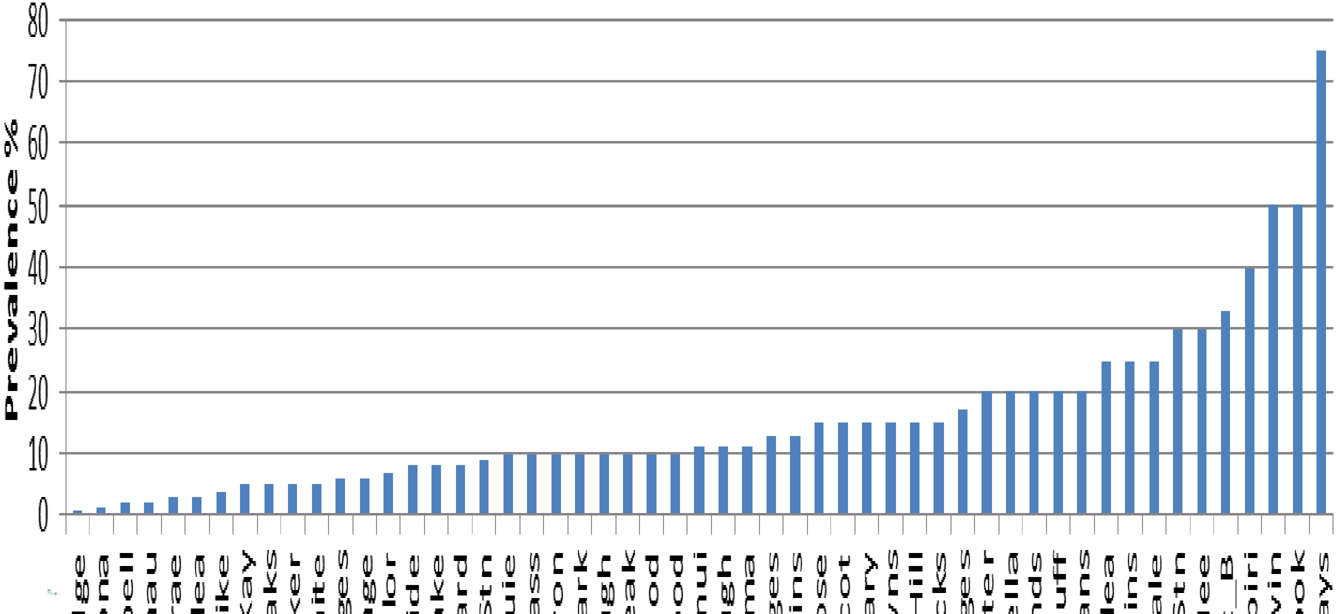
Predisposition/transmission

Field study
genetic variation
Virulent Footrot

72 flocks inspected
Predominantly
Merino/Merino types

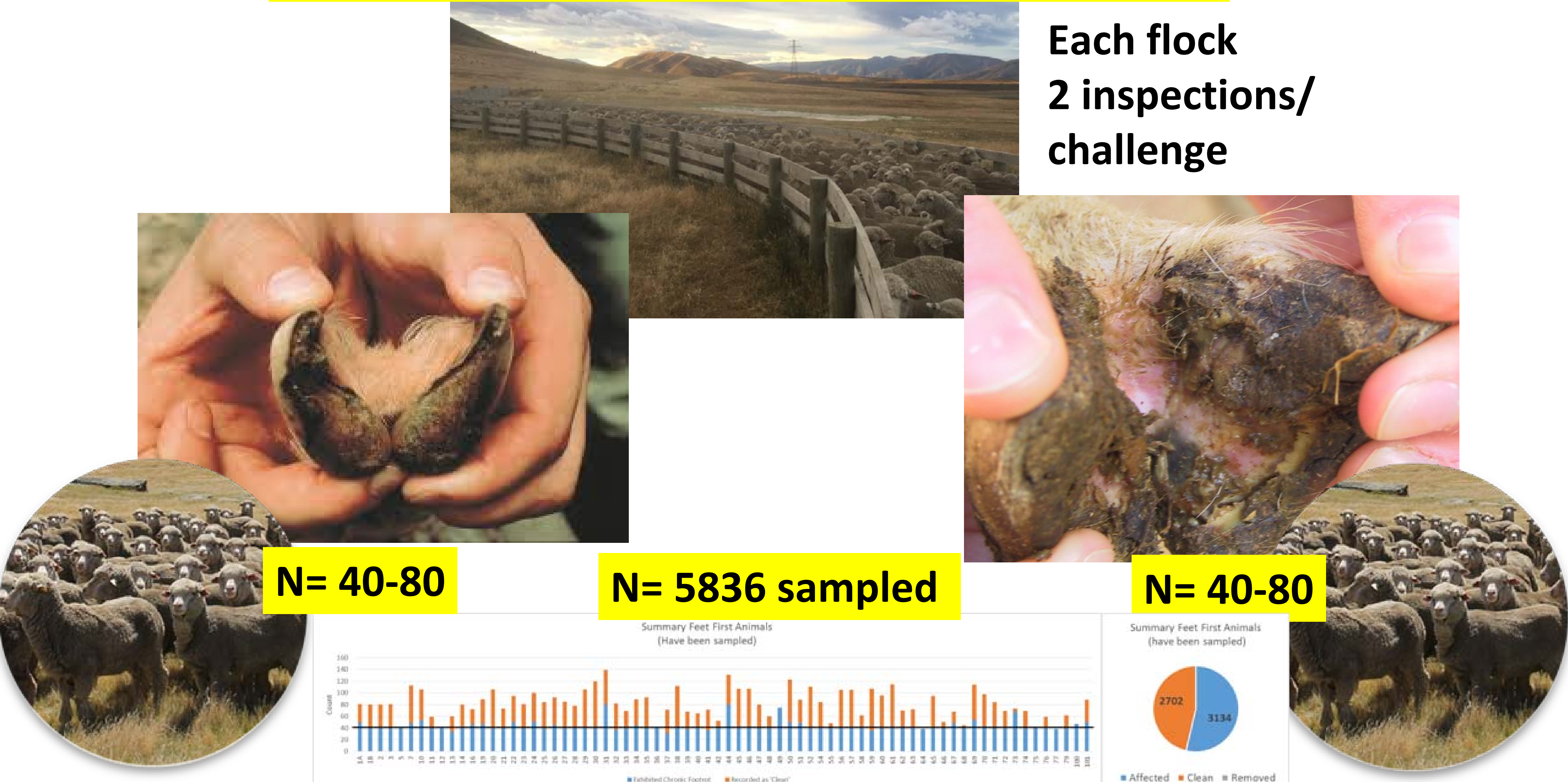


Footrot scores and flock prevalence



Sampling Case-Control

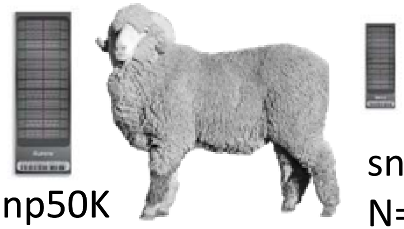
Each flock
2 inspections/
challenge



N= 40-80

N= 5836 sampled

N= 40-80



snp50K
N= 4,178

snp15K
N=830

Genotype 5,008 sheep & impute to 51,713 SNP after QC

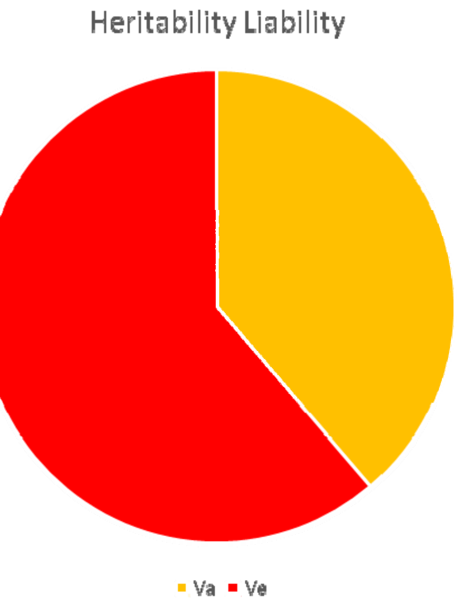
Final analyses- matched genotypes to phenotypes
Flock prevalence 30:70%, Merino types only
N=3,208 37 flocks

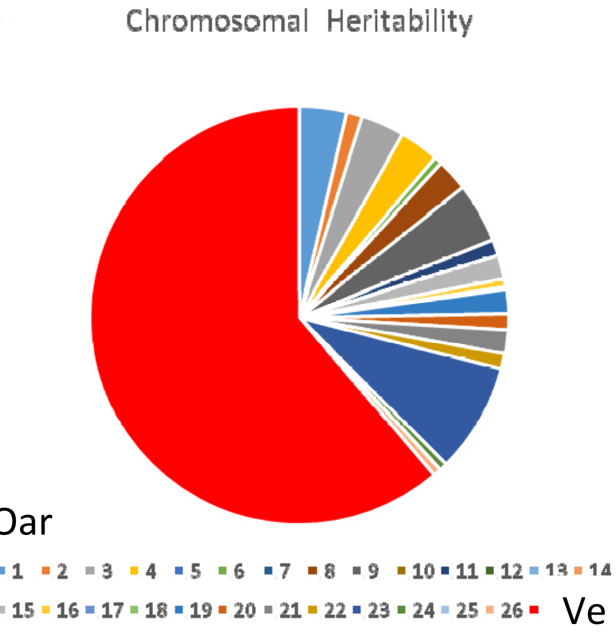
Model: logit FR (0,1)= Flock (observer), breed type, sex, age, GRM , residual

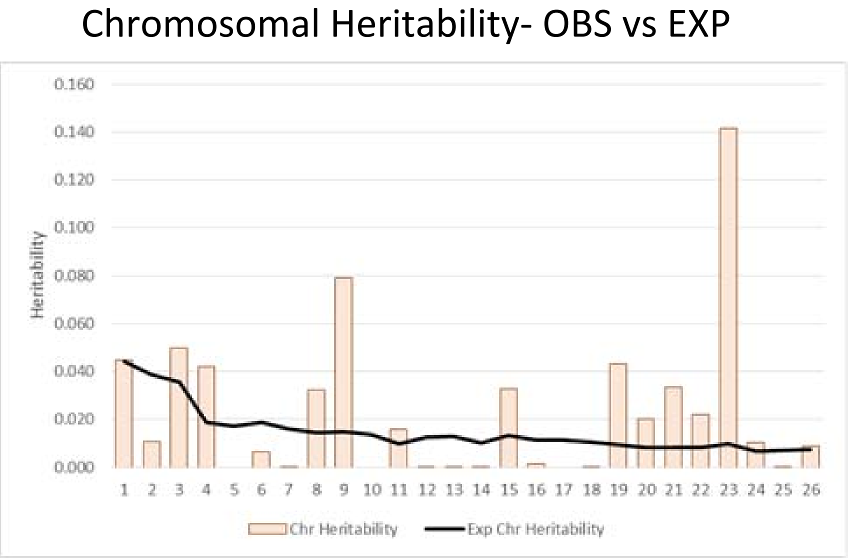
- Heritability
  - Chromosome Heritability
    - QTL location-GWAS
      - Positional candidate

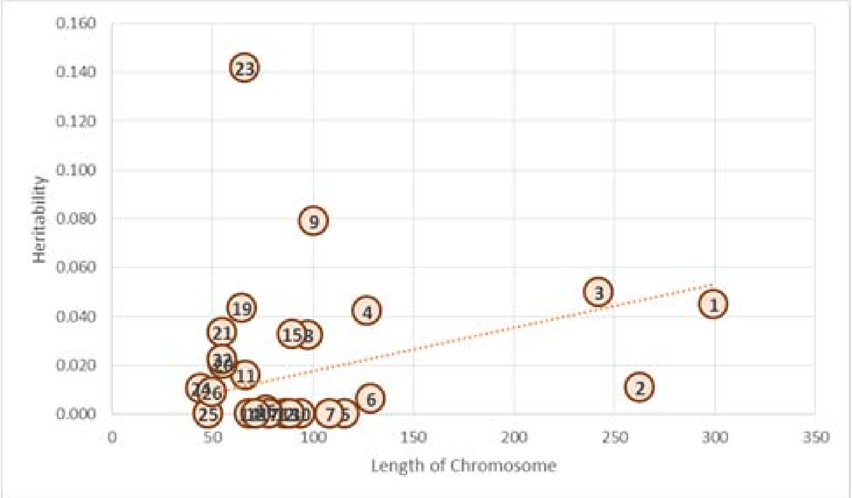
Chromosome Heritability – Case-Control

Heritability 0.41 (se0.04)



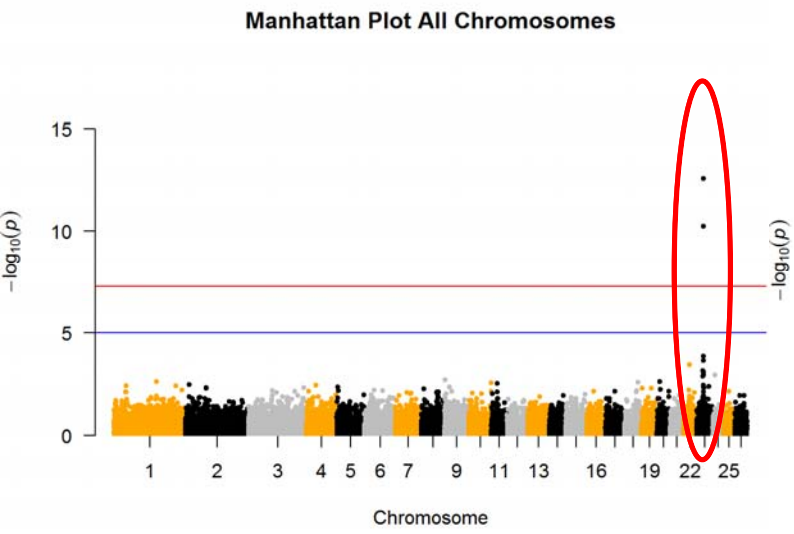


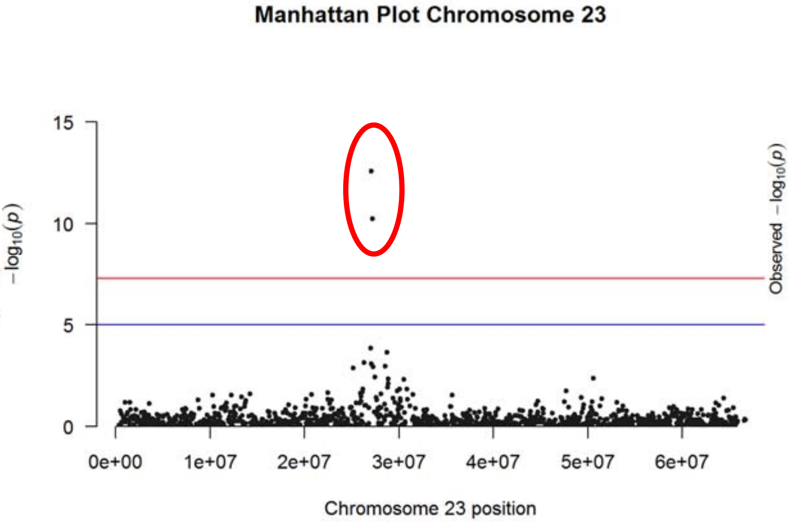


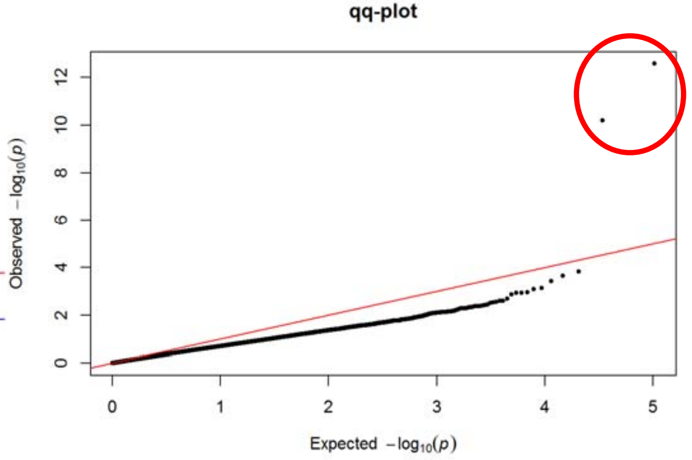


GWAS Outputs – Case / Control study

GRM = Fitted, Restricted to flock Ratio 30:70, fixed effects = flock, sex, breed, age class


Manhattan Plot All Chromosomes

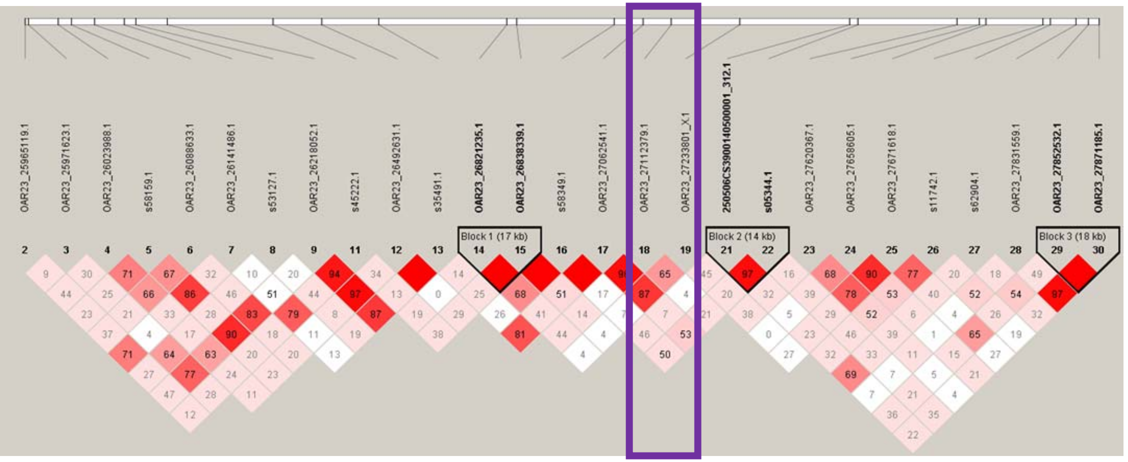

Manhattan Plot Chromosome 23


qq-plot

snp_num	snp_name	chromosome	position	snp_est	snp_est_err	t_value	p_value
48429	**OAR23_27112379.1**	**23**	**27112379**	**-0.1213420**	**0.0165304**	**-7.34051**	**2.663673e-13**
48430	**OAR23_27233801_X.1**	**23**	**27233802**	**0.1224890**	**0.0186583**	**6.56487**	**6.022067e-11**
48427	s58349.1	23	27011021	0.0678792	0.0178452	3.80377	1.450803e-04
48453	OAR23_28768759.1	23	28768759	0.0626619	0.0169762	3.69116	2.268262e-04
47319	OAR22_24529089.1	22	24529089	0.0656930	0.0184299	3.56447	3.697362e-04
48421	OAR23_26291258.1	23	26291258	-0.0557828	0.0164934	-3.38214	7.275714e-04

Haploview and impact of QTL markers

2 SNPs not close >>>> high likelihood of recombination between “key gene” & significant SNPS



Significant QTL but

Relatively small effect

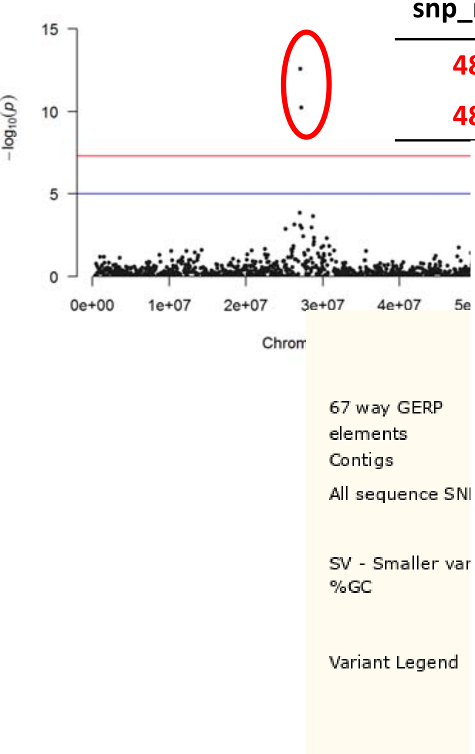
High Residual Va

Trait	Markers fitted	Oar 23 Heritability	se		Residual genome heritability	se		Full Genome heritability	se	
FR (0,1)	0 fitted	**0.14**	(0.04)		0.27	(0.05)		0.41	(0.04)	
FR (0,1)	2 fitted	**0.12**	(0.04)		0.27	(0.05)		0.39	(0.04)	

GWAS-positional candidates

GRM = Fitted, Restricted to flock Ratio 30:70, fixed effects = flock, sex, breed, age class

Manhattan Plot Chromosome 23



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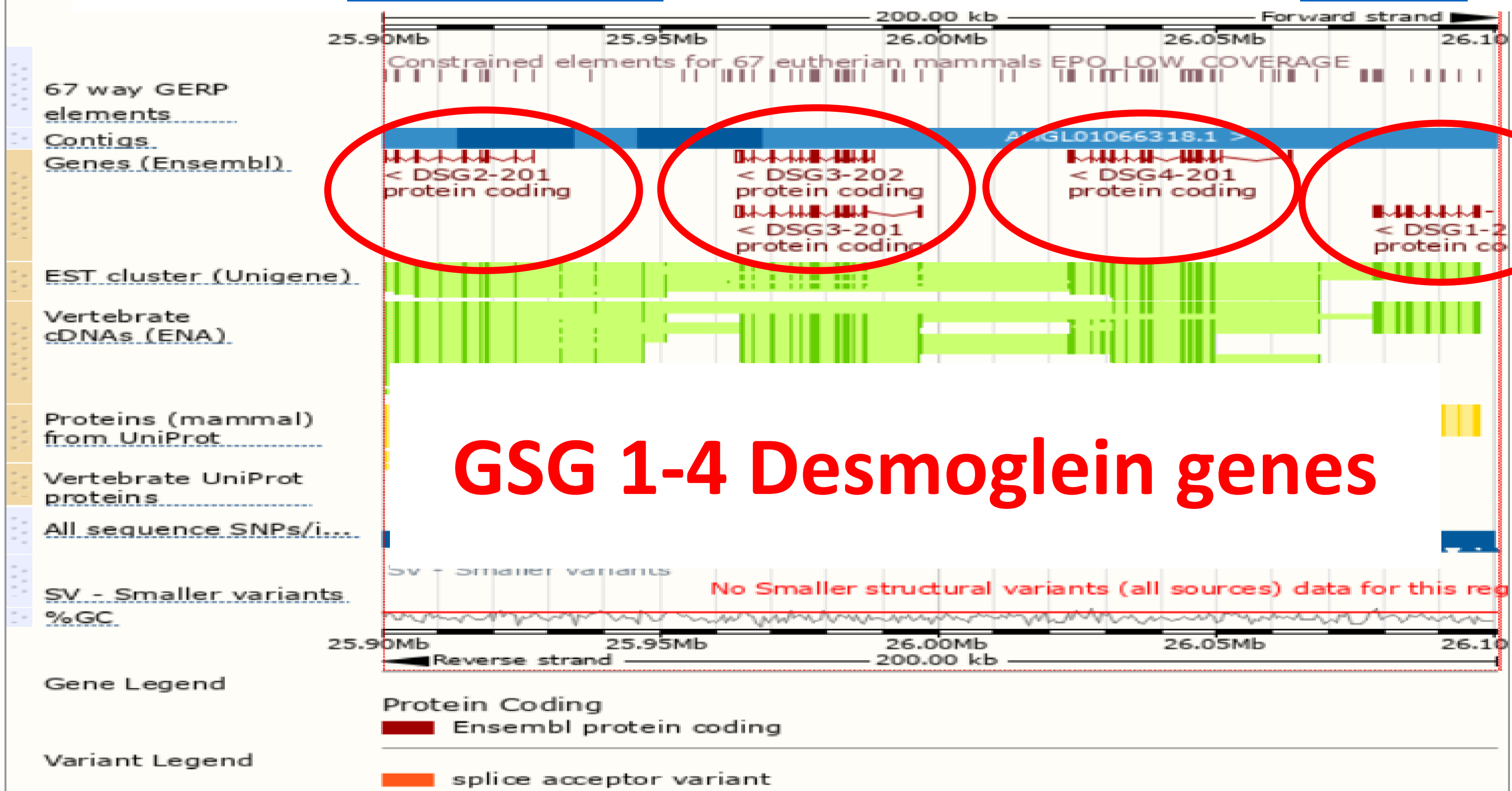
rs407911045 =OAR23:25972928 rs430746746 =OAR23:26109761



GSG 1-4 Desmoglein genes

DSG1-4 Candidate genes

OMIM

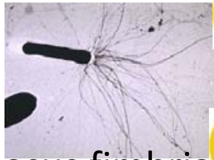
Online Mendelian Inheritance in Man

MGI

Mouse Genome Informatics

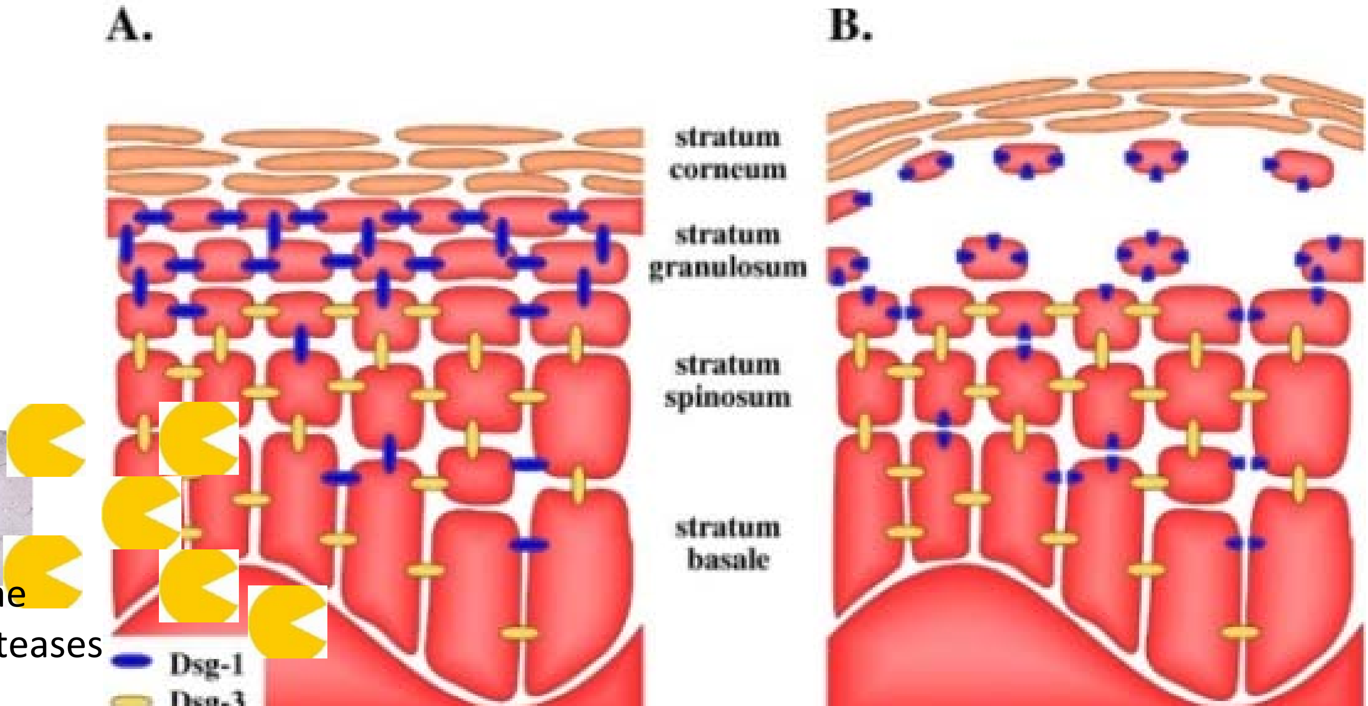
PubMed

Desmoglein genes



D nodosus fimbriae

proteases



Conclusions

- **Resistance Virulent FR - Heritable & polygenic**
    - **selective breeding Merino feasible**
- **Major QTL OAR23**
    - **but does not account for all variation**
    - **Needs validation & fine mapping**
- **Best option for gEBV – relationship+QTL+snp effects**
    - **See Walkom et al –these proceedings**
- **DSG gene family suitable candidates**

Acknowledgements

- NZ Merino inc, NZ Primary industries & New Zealand Merino Co $$$
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