

Genome-wide association study on meat tenderness using genotypes imputed to whole genome sequence in a diverse New Zealand sheep population

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Introduction

- Genotyping for DNA-based parentage and genomic selection is routine in the New Zealand sheep industry
- ~23,000 New Zealand sheep have been genotyped with the Illumina OvineHD BeadChip array (~600,000 SNPs)
- Imputation to whole genome sequence (WGS) offers the potential to identify causative variants associated with traits of economic importance to the sheep industry
- The sheep population in New Zealand is diverse, with over 50 purebred or composite breeds listed in the national database
- The International Sheep Genetics Consortium (ISGC) has a 1,000 Sheep Genomes Project — 935 individuals have WGS data (<https://www.sheephapmap.org/>)

Aim

Impute individuals with high density genotypes to whole genome sequence and evaluate the use of sequence variants for improved prediction of meat tenderness

Imputation

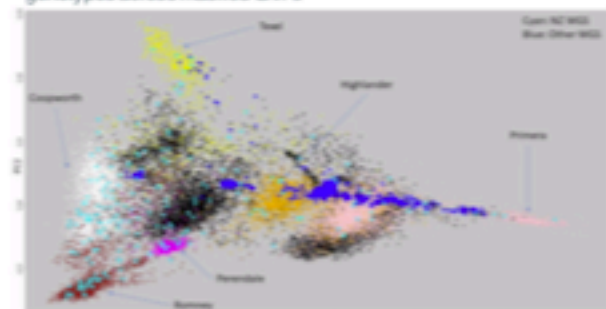
WGS Animals (n=935)		HD Animals (n=22,674)
Country	Breed	Primary Breed (pedigree)
• 302 Australia	• 292 Composite	• 2,729 Coopworth
• 213 New Zealand	• 124 Merino (Horned and Polled)	• 2,681 Friesian
• 95 Morocco	• 48 Romney	• 2,475 Highlander
• 38 United States	• 42 Coopworth	• 2,364 Romney
• 21 Iran	• 42 (Polled) Dorset	• 909 Texel
• 76 Other	• 387 Other	• 11,496 Other

Filtering of WGS Variants

- Kept all SNPs on HD chip as long as:
 - Reference/alternate alleles match WGS variants
 - Concordance > 0.95 (123 individuals had both HD and WGS)
- Average depth between 4 and 25
- QUAL > 30 & Average Genotype Quality > 30
- Call rate > 0.99; MAF > 0.01
- Non-HD genotypes LD pruned if $r^2 > 0.95$
- Final: 24,257,248 SNPs (457,434 on HD)

Imputation Approach

- Phasing/Imputation of Chromosome 26 in Beagle 5.1
 - Default parameters except Ne = 500
- Masked 759 SNPs in HD animals
- Imputed to 505,190 WGS variants
- Individual accuracy: concordance between true and imputed genotypes across masked SNPs



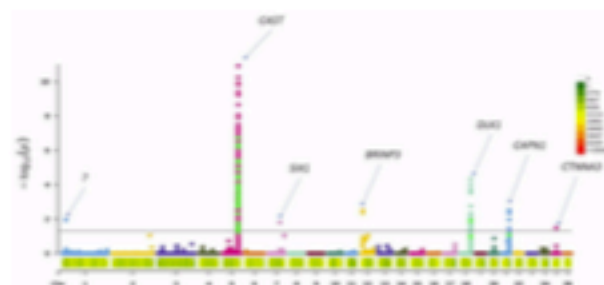
PCA Plot of Animals with HD and WGS Genotypes (HD genotypes)

Imputation Accuracy

- NZ WGS Animals as reference: 0.958
- NZ and AUS WGS Animals as reference: 0.969
- All WGS Animals as reference: 0.972
- Similar Imputation accuracy was observed for different breeds

GWAS

- GWAS on meat tenderness using BOLT-LMM (n=10,146)
 - $h^2 = 0.27 \pm 0.02$
 - FDR Control using Benjamini-Yekutieli
 - 901 significant markers used for prediction



GWAS for Meat Tenderness. Light green points are HD SNPs.

Genomic Prediction

- Forward Prediction in ASReml
 - Train: 2010-2014 (n=9,361); Predict: 2015 (n=785)
 - Cor(Adjusted Phenotype, GBV)/ $\sqrt{h^2}$

Genomic Prediction Accuracy

- Single GRM (HD SNPs only): 0.35
- Single GRM (HD + WGS Significant SNPs): 0.37
- Two GRMs (HD SNPs, WGS Significant SNPs): 0.42

Discussion

- Imputation accuracy from HD SNPs to WGS variants was reasonably high, indicating the WGS animals capture haplotypes present in the New Zealand sheep population
- Putative causal variants were identified in a GWAS for meat tenderness using WGS variants that were not found in a GWAS using HD SNPs
- Genomic prediction accuracy of meat tenderness was improved when incorporating putative causal variants from the GWAS using WGS
- After further validation, these putative causal variants could be used to improve the design of the available genotyping arrays

Conclusion

Imputation to whole genome sequence has the potential to improve genetic gain in the New Zealand sheep population