FINDING MAJOR GENE EFFECTS IN AUSTRALIAN MEAT SHEEP – FEASIBILITY STUDY FOR A TEXEL DATASET

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SUMMARY

Segregation analysis indicated the presence of major genes for three post-weaning traits; weight, eye-muscle depth and C fat, within a Texel based dataset obtained from LAMBPLAN. The effect of expressing one paternal copy (in phenotypic standard deviation units in brackets) was 2.71 kg (0.48) for weight, 1.05mm (0.50) for eye-muscle depth and -0.42mm (0.60) for C fat. Power calculations were used to determine the family sizes required to detect markers linked to these genes for both the halfsib (HS2) and grandprogeny (HS3) designs. Marker detection using the HS2 design required phenotypes on approximately 150 half-sibs, a feasable number within this breed.

Keywords: Major genes, Segregation analysis, Detection power, Sheep

INTRODUCTION

Finding molecular markers linked to major genes (or quantitative trait loci, QTL) should result in faster genetic improvement through marker assisted selection of young sires. The Australian prime lamb industry could particularly benefit from the development of this technology, especially when applied to carcass and meat quality traits that are important to consumer acceptance. There is some scope for cost efficient marker detection within this industry. Performance information from LAMBPLAN (Banks 1995) and knowledge of major gene regions in other species, especially beef cattle, can be utilised.

The ability to detect markers linked to major genes within an existing livestock population depends on the structure and size of families, the size of the effect of the major gene, and that the major gene is segregating within families. This study, through segregation analysis and power calculations, determines the feasibility of marker detection within a Texel based dataset obtained from LAMBPLAN. Texels were introduced to Australia in 1993 and are characterised by high percentatge lean. The traits considered were post-weaning weight (PWWT), post-weaning eye muscle depth (PEMD) and post-weaning C fat (PWCF).

MATERIALS AND METHODS

Data. The database was obtained from LAMBPLAN and included all purebred and part Texels, related animals and animals from the same contemporary groups. The data was limited to animals where ultrasonic measurements of subcutaneous fat depth and *Longissimus dorsi* depth at the 12th rib, along with weight, were recorded between 130-300 days of age by LAMBPLAN accredited

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personnel. The database numbered 10,107 animals with an additional 2,877 animals without records included in the pedigree. The majority of the animals were either purebred Texel (~27 %), half Texel (~20 %) or no Texel (~33 %), with the balance varying proportions of Texel. All animals with records were born between 1993 and 1997. Sire identities were recorded for about 90 % of the individuals and dam identities recorded for about 50 %. Total dams numbered 2,840 and total sires 705. Of animals with records the number of dams was 2,432 with an average progeny group size of 1.8, and the number of sires was 367 with an average progeny group size of 25 (range 1 to 297). 23 sires had a progeny group size ≥100, and of these sires 16 were purebred Texels. Unadjusted trait means and standard deviations (in brackets) were 46.9 kg (10.0 kg) for PWWT, 27.4mm (3.9mm) for PEMD and 2.8mm (1.2mm) for PWCF.

Segregation analysis. The program 'Gene Detective' (pers. comm. B.Tier) was used to analyze the data. This program uses Markov Chain Monte Carlo methodology. The model contained random polygenic, fixed systematic and one major gene effect. Genotypes for the major gene, genotypic effects and polygenic and residual variances were estimated using single trait analysis. Estimates were from 1,000 samples preceded by 500 burn-in samples. Fixed effects for PWWT were post-weaning age, birth type (BT) as single versus multiple and contemporary group (CG). Fixed effects for PEMD were PWWT, BT and CG, and those for PWCF were PWWT and CG. CGs were based on sex, year, flock and lambing season. The effect of breed was not included in the model as breed was highly confounded with CG.

Power calculations. Power is the probability of detecting a marker linked to a major gene, for a certain level of type 1 error (where a type 1 error is a false positive). Two designs were considered; the half-sib design (HS2) where large half-sib families are generated and genotypes and phenotypes are required on all progeny, and the grandprogeny design (HS3) where genotypes are required on the male progeny of grandsires only (referred to as sons), and phenotypes on the progeny of these sons (Weller *et al.* 1990; Van der Beek *et al.* 1995). Power was determined for single marker analysis according to Weller *et al* (1990). Segregation analysis estimates of the size of major gene effects and heritabilities were used and a recombination frequency of 0.05 was assumed. Results are given for a single heterozygous sire, since sires likely to be heterozygous can be selected on the basis of 'Gene Detective' results.

RESULTS AND DISCUSSION

Segregation analysis. Table 1 shows posterior means and sampling standard deviations for variance estimates from the segregation analysis. Results support the presence of a major gene segregating within this dataset for each of PWWT, PEMD and PWCF. In each case the variance attributable to a major gene is significant ($P<0.001$). The effect of expressing one paternal copy (in phenotypic standard deviation units in brackets) was 2.71 kg (0.48) for PWWT, 1.05mm (0.50) for PEMD and -0.42mm (0.60) for PWCF. Results (not shown) indicated there was insufficient information on the dam side to determine the effect of expressing a maternal copy. Further, simulation studies using the existing pedigree (results not shown) confirmed that polygenic breed differences were not being interpreted as major gene effects.

Alleles increasing PWWT and PEMD, and decreasing PWCF are considered favourable. Animals with a >80 % probability of carrying 2 copies of the favourable allele (homozygous positives) numbered 3 for PWWT, 8 for PEMD and 10 for PWCF. Of these 1, 6 and 9 animals respectively were purebred Texels. However genotype probabilities of >0.8 generally stemmed from individuals with 100 or more offspring and purebreds sired the majority of the larger progeny groups. Three individuals were homozygous positive for more than one trait (PWCF and PEMD in each case).

Family sizes required to detect markers linked to major genes. Tables 2 and 3 give power of detection for the HS2 and HS3 designs respectively, for type 1 errors (α) of 0.05 and 0.01, and various family sizes. If marker choice was based on those already detected in other genetically related species, a complete genome scan is not required and the use of a higher type 1 error (0.05 and 0.01 as compared to 0.001) is valid. Considering power of 0.8 reasonable for marker detection a minimum of 150 half-sibs for PWWT and PEMD and 100 for PWCF are required for HS2 at α=0.05. For HS3 at α=0.05 reasonable power is obtained for 100 sons with 20 progeny each for PWWT and PEMD and 50 sons with 20 progeny each for PWCF. It should be noted that power calculations presented here are subject to the assumptions outlined in Weller *et al* (1990) and reliant on the accuracy of segregation analysis results.

Feasibility. For similar power, phenotypes are required on a much larger number of animals for the HS3 design as compared to the HS2 (for example, 1,500 versus 200 for PWWT). However, the HS3 design has lower genotyping costs and the logistical advantage that DNA is only required from sons. The largest half-sib families within this dataset were from 5 sires with between 200 and 350 progeny each. Of these one sire was heterozygous for all three traits. This sire is a purebred Texel and an ideal candidate for multi-trait analysis using the HS2 design. Family size and structure within this dataset was not sufficient for HS3 detection: the most promising grandsire had only 20 sons with progeny group sizes of 10 or more. Whilst some sons had larger progeny group sizes, maximum power for traits with high heritability is achieved for the HS3 design when the grandsire has many sons, with less emphasis on the number of progeny per son (Weller *et al.* 1990). Generation of the large numbers of progeny required for HS3 would cause inbreeding concerns within this breed with a relatively small population.

By using outcross populations for QTL analysis, as opposed to designed crosses, results are more applicable to current breeding populations. Use of segregation analysis to source sires from an outcross population gives prior knowledge on sire heterozygosity, thus minimising detection costs. If molecular markers linked to the major genes identified here are found, marker genotypes can be used to aid selection decisions.

Table 1. Means and sampling standard deviations ( ) for major gene, polygenic and error variances for post-weaning weight (PWWT), eye muscle depth (PEMD) and C fat (PWCF)

Trait	Major gene variance (V_q)	Polygenic variance (V_a)	Error variance (V_e)	Proportion of variance described by major gene[A]	Polygenic heritability[B]
PWWT	2.12 (0.66)	13.64 (2.11)	15.72 (1.35)	0.067	0.43
PEMD	0.29 (0.07)	1.87 (0.22)	2.30 (0.15)	0.065	0.42
PWCF	0.05 (0.01)	0.18 (0.03)	0.27 (0.02)	0.096	0.37

[A] $V_q / (V_q + V_a + V_e)$
[B] $V_a / (V_q + V_a + V_e)$

Table 2. Power of detection per sire for markers linked to major genes for the halfsib (HS2) design

Number of progeny	Power with type 1 error[A]			
	PWWT PEMD		PWCF	
	0.05	0.01	0.05	0.01
250	0.95	0.86	0.99	0.97
200	0.90	0.75	0.98	0.92
150	0.81	0.60	0.93	0.81
100	0.64	0.39	0.80	0.60

[A] Heritabilities used for power calculations are listed in Table 1 and the size of the major gene effect used was that given for one paternal copy.

Table 3. Power of detection per grandsire for markers linked to major genes for the grandprogeny (HS3) design

Number of sons	Progeny per son	Total progeny	Power with type 1 error [A]			
			PWWT PEMD		PWCF	
			0.05	0.01	0.05	0.01
150	20	3000	0.96	0.88	0.99	0.99
	10	1500	0.90	0.74	0.98	0.94
100	20	2000	0.87	0.69	0.98	0.92
	10	1000	0.75	0.53	0.92	0.78
50	20	1000	0.58	0.34	0.80	0.59
	10	500	0.46	0.24	0.66	0.42

[A] Heritabilities used for power calculations are listed in Table 1 and the size of the major gene effect used was that given for one paternal copy.

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