Sequence variations in the growth hormone and insulin-like growth factor 1 genes are associated with body size traits in Holstein-Friesian dairy cattle

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Introduction Feed costs make up a large proportion of the variable costs in dairy herds and a large proportion of the feed costs are attributable to maintenance which is influenced by animal size. Molecular markers associated with smaller body size but not antagonistic to performance would be useful to select for more efficient animals. The growth hormone (*GH*) and insulin-like growth factor 1 (*IGF-1*) genes were selected in this study as candidate genes for body size because of their known role in animal growth and development. The objective of this study was therefore to discover novel SNPs in these genes and to quantify their association with body size related production traits in dairy cattle.

Material and methods A panel of 22 cattle (four Belgian Blue crossbreds, four Charolais, four Simmental, four Aberdeen Angus crossbred and six Holstein-Friesians) was selected for SNP discovery. Regions of the *GH* and *IGF1* genes encompassing both promoter and regulatory flanking sequences were PCR amplified and sequenced. Sequence validation and *de novo* polymorphism detection was carried out using a combination of software packages including BLAST, ClustalW and Chromas. Identified SNPs were then genotyped across 848 HF sires with progeny in Ireland. The association between each SNP and performance was quantified using weighted mixed models in ASREML (Gilmour *et al*., 2009) with genotyped individual included as a random effect. Year of birth (divided into five yearly intervals) and percent Holstein of the individual sire were included as fixed effects in the model. In all instances the dependent variable was de-regressed PTA for calving interval and functional survival, weighted by their respective reliability less the parental contribution. Genotype was included in the analysis as a continuous variable. A multiple regression model was developed within each gene separately by backward elimination of non-significant ($P > 0.05$) SNPs.

Results Sequence analysis of ~ 13 kb across these two genes identified; 44 *de novo* SNPs in the *GH* gene and nine *de novo* SNPs in the *IGF-1* gene. Significant associations were found with both novel and previously identified SNPs across both genes with growth traits (Table 1). For example: in the *GH* gene, a C to T substitution in *GHi32,* was associated with increased carcass conformation of 0.05 (scale 1 to 15)*;* and in the *IGF-1* gene a substitution of the A allele with a G allele in *IGF1i4* was associated with increased cull cow weight of 2.61 kg and an increase of carcass weight of 2.41 kg (SE= 1.01 kg). No SNP was associated with animal stature.

Table 1 Allelic substitution effects (standard errors in parenthesis) between SNPs in the *GH* and *IGF1* genes and carcass conformation (Conform; scale 1 to 15), carcass fat (Cfat; scale 1 to 15), cull cow weight (Cull; kg) and the body size linear type traits, body depth (BD), chest width (CW), body condition score (BCS) and angularity (ANG) expressed in standard deviation units (×100)

SNP[a]	dbSNP	Allele	Conform	Cfat	BD	CW	BCS	Cull	ANG
Igf1i2	*de novo*	C→T		5.14 (1.77)		-0.24 (0.11)			
Igf1i4	*rs29012855*	A→G						2.61 (1.29)	
Igf1i6	*de novo*	A→G					0.42 (0.21)	-3.40(1.50)	
Igf1r10	*de novo*	C→T				-0.51 (0.23)			
GHi63	*rs41916256*	A→T		4.46 (1.84)					
GHi36	*rs41923523*	C→T			22.88 (8.65)				0.19 (0.09)
GHi32	*de novo*	C→T	5.04 (1.95)						
GHi1	*rs41923485*	C→T							0.35 (0.17)
GHr17	*rs41923483*	C→T			36.86 (12.13)				
GHr19	*rs41923481*	C→T					-0.22 (0.09)		
GHr21	*rs41923479*	A→G			-44.86 (13.31)				
GHr24	*de novo*	C→T		5.44 (1.99)					

[a] :*GHrX* = SNP X located downstream i.e. 3' of the *GH* gene, *Igf1iY* = SNP Y located within an intron of the *IGF-1* gene.

Conclusion Analysis of the *GH* and *IGF-1* genes has identified SNPs associated with traits related to body size, reaffirming previous studies reporting their involvement in animal growth and development.

References
Gilmour, A. R., Cullis, B. R., Welham, S. J. and Thompson, R. 2009. ASREML Reference Manual 2nd edition.