

DNA profiling makes it practical to select for or against increased muscling.

The myostatin gene (GDF-8) was one of the first identified genes proven to have a large effect on an economically important trait.¹ Myostatin normally prevents excessive muscular development. Therefore, changes (mutations) in the gene lead to reduction or loss of function. Forms of these genetic mutations have a large effect on muscle mass and been associated with the phenotype described as “double-muscling.” They also have been associated with heavier birth weights, heavier weaning weights and higher yield of lean.²

Some breed associations treat the calving difficulties associated with double-muscling as a genetic defect that needs to be eliminated³ while another (Piedmontese) makes myostatin genotype status a mandatory registration requirement and proudly calls themselves “the Myostatin Beef Breed.”⁴

Whether a producer considers the effects of the myostatin gene desirable or not, it is now practical for producers to identify the presence of a range of myostatin mutations by using the myostatin analysis as part of the IGENITY[®] profile.

BACKGROUND

Discovered by Johns Hopkins University scientists in 1997, myostatin is a member of the family of secreted growth and differentiation factors that are essential for proper regulation of muscle mass.⁵ Following the initial findings in mice, the gene also was localized in other species and numerous distinct mutations were identified.²

Considerable research has been conducted in the last few years to characterize the various myostatin mutations

present in cattle. A study involving 678 animals from 28 European beef breeds genotyped at the myostatin locus revealed a total of 20 different genotype combinations.⁶ Additional research at the U.S. Meat Animal Research Center has further characterized two of the most common myostatin mutations in Piedmontese (C313Y) and Belgian Blue (nt821 del11).^{2,7,8}

See inside for a summary of research conducted on the effects of myostatin mutations and tools available for analysis.

EXAMPLES OF THE IMPACT OF MYOSTATIN MUTATIONS

In cattle, myostatin affects traits of economic importance, including weight, muscling and calving difficulty.¹

- It has been suggested that calving difficulty may be a function of the dam’s genotype as well as that of the calf.¹
- A myostatin mutation has been associated with early life mortality, and calves with two copies of this mutation are especially susceptible to harsh conditions at birth.²
- In one study, animals with two copies of a myostatin mutation were heaviest at birth, were leaner and had a higher proportion of muscle mass; heterozygous animals were heaviest at weaning and had the highest live weight; and animals with zero copies had the highest fat content.²
- Production systems that can select for calves with one copy of certain myostatin mutations will benefit from heavier weaning weights and higher yield of lean, compared with cattle with zero copies.²



MYOSTATIN ANALYSIS AND IMPACT OF COMMON MUTATIONS

The myostatin analysis, as part of the IGENITY profile, detects nine different mutations of the myostatin gene. Research suggests that these changes are breed-specific.⁶

Of the nine mutations, six cause double-muscling and are referred to as “disruptive.” Animals that are homozygous (two copies) for any one of these six variations tend to have larger birth weights, increased dystocia, reduced fat cover, larger longissimus muscle (ribeye) area and enhanced meat tenderness.¹⁻¹¹

The other three mutations are referred to as “missense.” They yield increased muscularity and a reduction in external and intramuscular fat with no effect on birth weight or dystocia. Animals that are heterozygous for this mutation are typically intermediate for carcass muscling and fat.¹⁻¹¹

COMMON MUTATIONS IDENTIFIED IN THE IGENITY PROFILE

<u>Disruptive Mutations</u>	<u>Associated Breed(s)</u>
C313Y*	Piedmontese
E226X	
E291X	
nt419	
nt821*	Belgian Blue, South Devon
Q204X	

<u>Missense Mutations</u>	<u>Associated Breed(s)</u>
D182N	
F94L*	Limousin
S105C	

*These three myostatin mutations are by far the most prevalent myostatin mutation in beef breeds found in the United States.^{2,6,9}

REVIEW OF RESEARCH ON THE IMPACT OF MYOSTATIN MUTATIONS

Tables 1 through 6 summarize published research on the effect of zero, one and two copies of the myostatin mutations for C313Y, nt821 and F94L on birth weight, dystocia, subcutaneous fat, intramuscular fat, longissimus muscle area and tenderness.

Table 1. Myostatin gene mutations and birth weight

BIRTH WEIGHT						
Mutation	Trait	Number of Mutated Alleles			Population/Animals	Reference
		0	1	2		
nt821(del11)	birth weight	40.2 ^a	42.2 ^b	–	Sires Charolais Dams crossbred	Casas et al., 2004 ²
		38.0 ^a	40.0 ^b	44.6 ^b	Sire Belgian Blue x British breed Dams crossbred	
C313Y	birth weight	X ^a	X+3.2 ^b	X+3.9 ^b	Sires Piedmontese (P), P X Angus (PA) or P X Hereford (PH) Dams PA or PH	Casas et al., 1999 ⁹
		35.7 ^a	37.0	40.1 ^b	F2 (Piedmontese X crossbred cows)	Short et al., 2002 ⁷
F94L	birth weight	No significant effects			Limousin X Jersey and Jersey X Limousin backcross progeny	Esmailzadeh et al., 2008 ⁸

Research summary: Birth weight

Calves homozygous for the nt821(del11) mutation (-/-, Belgian Blue origin) are significantly heavier at birth than calves homozygous for the wild type allele (+/+) while heterozygous calves are only slightly heavier than the latter.² Piedmontese crossbred calves homozygous for the C313Y mutation (-/-) are heavier at birth than calves homozygous for the wild type allele (+/+).^{7,10} The birth weight of heterozygotes (+/-) for the C313Y mutation is slightly higher than that of calves homozygous for the wild type allele (+/+) and does not cause additional calving problems. Birth weight, in Limousin X Jersey and Jersey X Limousin backcross progeny, is not associated with the F94L genotype.⁹

Table 2. Dystocia score (ds)/calving difficulty score (cds)/proportion difficult calvings (pdc)

CALVING/DYSTOCIA						
Mutation	Trait	Number of Mutated Alleles			Population/Animals	Reference
		0	1	2		
nt821(del11)	cds	1.15 ^a	1.24 ^a	1.80 ^b	South Devon	Wiener et al., 2002 ⁵
C313Y	pdc	X ^a	X+5 ^b	X+24 ^b	Sires Piedmontese (P), P X Angus (PA) or P X Hereford (PH) Dams PA or PH	Casas et al., 1999 ⁹
	ds-h*	1.24 ^a	1.85	2.20 ^b	F2 (Piedmontese X crossbred cows)	Short et al., 2002 ⁷
	ds-c*	1.01	1.00	1.08		
	pdc-h	12.9 ^a	43.1 ^a	49.6 ^b		
pdc-c	0.8 ^a	0.1 ^a	7.9 ^b			

Research summary: Calving difficulty

In the South Devon breed, calves homozygous for nt821(del11) cause significantly more dystocia. However, the heterozygous calves (+/-) are typically born without more difficulty than calves homozygous for the wild type allele (+/+).¹ In a study, differences in calving difficulty among Piedmontese calves possessing zero or two copies of the C313Y inactive mutation were reported.¹⁰ In crossbred heifers, but not in crossbred cows, the increased birth weight noted previously for C313Y was associated with more calving difficulty.⁷

FAT DEPTH/FAT COVER						
Mutation	Trait	Number of Mutated Alleles			Population/Animals	Reference
		0	1	2		
nt821(del11)	fc	4.75 ^a	4.75 ^a	1.25 ^b	Asturiana de los Valles	Aldai et al., 2006 ¹¹
	fd-mm	32.40 ^a	28.83 ^a	23.80 ^b	South Devon	Wiener et al., 2002 ²
	fd-cm	1.10 ^a	0.82 ^b	–	Sires Charolais Dams crossbred	Casas et al., 2004 ²
		1.26 ^a	1.06 ^b	0.43 ^c	Sire Belgian Blue X British breed Dams crossbred	
C313Y	fd-mm	6.3 ^a	5.6 ^b	2.6 ^b	Sires Piedmontese, Limousin, Hereford Dams crossbred	Short et al., 2002 ²
F94L	fd	0 to 2 associated with a significant decrease of fat depth at 600 days (a = -13.9%)			Limousin X Jersey and Jersey X Limousin backcross progeny	Esmailzadeh et al., 2008 ⁹

Research summary: Fat thickness

All four nt821(del11) studies noted in Table 3 reported significant differences between animals with zero versus two copies of the inactive myostatin allele. However, only one study, involving Belgian Blue sires mated to British breed dams, found the heterozygotes to be significantly different from both homozygotes. In a genetically highly diverse F₂ population of crossbred cattle of Piedmontese origin,⁷ a significant difference in fat thickness between animals with zero or two copies of the inactive C313Y allele was observed. Another study reported Limousin X Jersey crossbreds with two copies of the F94L mutation have significantly less subcutaneous fat than animals with zero copies.⁹

INTRAMUSCULAR FAT/MARBLING						
Mutation	Trait	Number of Mutated Alleles			Population/Animals	Reference
		0	1	2		
nt821(del11)	ms	544 ^a	482 ^b	–	Sires Charolais Dams crossbred	Casas et al., 2004 ²
		549 ^a	498 ^b	380 ^b	Sires Belgian Blue X British breed Dams crossbred	
	imf	1.90 ^a	1.80 ^a	0.94 ^b	Asturiana de los Valles (in <i>Longissimus thoracis</i>)	Aldai et al., 2006 ¹¹

Research summary: Intramuscular fat

In a study evaluating the impact of the nt821(del11) mutation in two different Belgian Blue X populations,² nt821 (del11) had a significant negative effect on marbling score. The other study reported a similar association, although only the homozygotes were significantly different.¹¹ Similarly, in a study of F94L in Table 3, significant differences between animals with zero or two copies of the F94L myostatin mutation were observed.⁹

LONGISSIMUS MUSCLE AREA (cm²)						
Mutation	Trait	Number of Mutated Alleles			Population/Animals	Reference
		0	1	2		
nt821(del11)	lma	89 ^a	99 ^a	–	Sires Charolais Dams crossbred	Casas et al., 2004 ²
		90 ^a	96 ^b	106 ^b	Sires Belgian Blue X British breed Dams crossbred	
C313Y	lma	74.3 ^a	86.4 ^b	109 ^b	Sires Piedmontese, Limousin, Hereford Dams crossbred	Short et al., 2002 ²

Research summary: Longissimus muscle area

Research in Table 5 clearly demonstrates the positive impact of nt821 (del11) on longissimus muscle area.² Moreover, C313Y and F94L^{7,9} also are associated with greater longissimus muscle area. In general, longissimus area increases with an increasing number of copies of the inactive form of all three mutations.

MEAT TENDERNESS						
Mutation	Trait	Number of Mutated Alleles			Population/Animals	Reference
		0	1	2		
C313Y	mte	5.8	6.2	6.5	Piedmontese crossbreds (Ratings on a scale from 1 to 8: 1 = extremely tough, extremely difficult, abundant, extremely dry, and extremely bland; 8 = extremely tender, extremely easy, none, extremely juicy, and extremely intense)	Wheeler et al., 2001 ¹
	efr	5.9	6.4	6.6		
	act	6.3	6.6	6.9		
	jui	5.6	5.6	5.4		
	bfi	4.7	4.7	4.6		

Research summary: Tenderness

The study in Table 6 evaluated the impact of the C313Y myostatin mutation on three tenderness components, plus juiciness and flavor intensity of several muscles, including the longissimus.⁸ Significant differences between the homozygotes were observed for all three tenderness components and juiciness. No differences existed for beef flavor intensity. In that same study, cooking temperature also increased (meat cooked slightly faster) as inactive myostatin alleles increased. No significant difference in tenderness was reported for Limousin cross animals with more copies of the F94L inactive mutation.⁹

CONCLUSIONS.

The ability to identify the presence of various myostatin mutations can provide a powerful tool to help select either for or against this phenotype directly at the genotypic level. The myostatin analysis, as part of the comprehensive IGENITY profile, evaluates nine different mutations and presents results in a form that can be applied to seedstock and cow/calf systems.

The comprehensive IGENITY profile analyzes nine myostatin mutations. And much more.

Only IGENITY offers the most powerful profiling technologies with user-friendly applications and consultation. The comprehensive IGENITY profile empowers producers to make more confident real-time decisions and higher-quality, more profitable products.

IGENITY works with research partners around the globe to continue to discover and integrate innovative technologies, and enhance the value of the IGENITY profile. At press time, IGENITY offered analyses related to the following economically significant traits:

- Residual feed intake
- Average daily gain
- Tenderness
- Marbling
- Quality grade
- Yield grade
- Fat thickness
- Ribeye area
- Heifer pregnancy rate
- Stayability (longevity)
- Calving ease
- Docility
- Myostatin
- Arthrogyrosis Multiplex
- Coat color
- Breed-specific horned/polled
- Multisire parentage
- BVD-PI diagnostic test

As IGENITY advances the science of DNA technology, more analyses will be added.
For the latest information about the IGENITY profile, visit www.igenity.com or call 1-877-IGENITY.

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⁴Piedmontese home page. Available at: <http://www.piedmontese.org/homepage-NAPA.html>. Accessed November 24, 2008.

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⁶Dunner S, Miranda ME, et al. Haplotype diversity of the myostatin gene among beef cattle breeds. *Genet Sel Evol.* 2003;35:103-118.

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⁸Wheeler TL, Shackelford SD, et al. The effects of Piedmontese inheritance and myostatin genotype on the palatability of longissimus thoracic, gluteus medius, semimembranosus and biceps femoris. *J Anim Sci.* 2001;79:3069-3074.

⁹Esmailizadeh AK, Bottema CDK, et al. Effects of the myostatin F94L substitution on beef traits. *J Anim Sci.* 2008;86:1038-1046.

¹⁰Casas E, Keele JW, et al. Quantitative analysis of birth, weaning and yearling weights and calving difficulty in Piedmontese crossbreds segregating an inactive myostatin allele. *J Anim Sci* 1999;77:1686-1692.

¹¹Aldai N, Murray BE, et al. The influence of breed and mh-genotype on carcass conformation, meat physico-chemical characteristics, and the fatty acid profile of muscle from yearling bulls. *Meat Science.* 2006;72:486-495.



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