The Role of Myostatin on Growth and Carcass Traits and its Application in Animal Breeding

Seyed Ziaeddin Mirhoseini, Jalal Zare

[1.] Department of Animal Science, University of Guilan, Rasht, Iran
szmirhoseini@gmail.com; mirhosin@guilan.ac.ir

Abstract: Myostatin or growth and differentiation factor 8 (GDF8), is a regulator factor that determines muscle mass. Mutation in the myostatin sequence controls its regulating function and results in growth and hypertrophy of muscles. Mutation in myostatin has been found in various species and this gene has three exons and two introns in all spices. Muscular hypertrophy is found in Belgians-Blue cattle, and animals with mutant allele produce more meat. Mutant allele with the growth rate and desired carcass traits are significant correlated and increase ratio the muscle to fat and bone.Various SNPs in myostatin have been found which have an important association with carcass. SNP g + 6223 G>A used as an effective marker in Texel sheep. Severe selection of mutated allele in European breeds has caused these allele become fixed in the population. Whereas, in Iranian breeds frequency of this allele is very low and its reason comes back to the genetic background and selection programs.

[Mirhoseini SZ, Zare J. **The Role of Myostatin on Growth and Carcass Traits and its Application in Animal Breeding**. *Life Sci J* 2012;9(3):2353-2357] (ISSN:1097-8135). http://www.lifesciencesite.com. 340

Keywords: carcass trait, myostatin, Muscular hypertrophy, SNP, meat quality

1. Introduction

Still produce meat are most important animal production. Not only quality but quantity is important in meat industry as well. Food and physiological research demonstrated even meat macro molecular components have a great influence on quality. Scientists in the past decade many techniques for identifying and determining the origin of species, especially in meat products are identified that is very important in respect to economic, religious and health (Ghovvati et al., 2009).

Advances in molecular genetics caused identification many genetic markers, these markers help to identify quantitative trait loci (QTL) related to economical traits. If polymorphisms created in marker affects on gene function or have a linkage with QTL, the marker shows the maximum efficiency. Genome scans in economic animal show QTLs that are effective on growth and carcass traits. Wide studies have been conducted in the sequence of genes associated with economic traits. Polymorphisms that are associated with the function of these genes have been observed in different species.

Myostatin is an effective gene for growth and function as an inhibitor factor on muscles growth (Figure 1). Different polymorphisms have been identified in the sequence of this gene that has a significant association with growth and carcass traits. These polymorphisms are used as efficient marker in beef cattle in order to increase quality and quantity of meat.

Muscular hypotrophy was observed in a few cattle breeds and it's due to the mutation of myostatin. Mutation has been fixed in these breeds and it's transmitted from one generation to another. These animals have a big and bulky body and this phonotype is recognizable easily so, they are the source of meat production.

The beef cattle of Belgian-blue are homozygote for these mutations. Because the aim of breeding of this breed is selecting and reproduction animals with muscle hypertrophy (Figure 2) (McPherron and Lee, 1997).

Identification of effective QTL on double-muscled in different species

The genetic cause of muscular hypertrophy was unknown for a long time. When the changes of myostatin gene were discovered on mouse, QTL related with double muscled animals was identifying (McPherron et al., 1997). When was discovered genetic cause of double muscled was cleared that this trait is probably autosomal, partially recessive and incomplete penetrance (McPherron et al., 1997).

After that wide researches began on different cattle breeds and using FISH method determined that this gene is located in the q arm of chromosome 2 close to the centromere region and its locus was named *mh* (Smith et l., 1997). Then by the use of molecular methods was characterized an 11-bp deletion mutation within 3 exon of myostatin in Belgian Blues breed. This mutation is considered as marker for double muscling, so different genotypes of *mh* locus in cattle can apply for genetic selection (Bellinge et al., 2005).

Early studies show that, there is an effective QTL for fatness and muscle size on chromosome 2 of sheep. Identify of Mutation in this QTL was a new start in breeding of carcass traits (Walling et al., 2004).

In Texel sheep, identify a selective sweep at myostatin that located on chromosome 2 was used for mapping QTL effective for increase muscle mass. In this survey mutation of G→.A in nucleotide 1232, after a stop codon was identified and it causes muscular phonotype. (Clop et al., 2006).

Physiological comparison of normal animals and double muscling (DM)

Earliest studies on double-muscling animals indicated that mouse with compact phonotype and double-muscling have internal organs like: heart, kidney and intestine bigger than normal animal (Buenger et al., 2004).

Animals with double muscle phenotype have the increase in the diameter of the muscle filaments and increased number of filaments (hypertrophy and hyperplasia). But this increase is not exactly twice that of normal animals. Also, these animals are having less collagen. Reported that the connective tissue of these animals are less than the normal animals (Kobolak and Gocza, 2002). In addition, survey of circulating hormones has been found that higher growth hormone levels were found in DM cattle compared with normal animals. A similar result was found for insulin, creatine and creatine and muscle IGF2 mRNA concentration. Level these hormones with normal animals higher than DM cattle (Gerrard et al., 1991).

The amount of fat in the carcass of DM cattle is significantly less than normal cattle, especially intramuscular fat (marbling) is significantly influenced by DM phonotype because reduced subcutaneous and internal fat tissues. Study the carcass of Belgian blues shows that fat compounds is quite different with other normal breeds.

When the whole content of lipid and percentage of unsaturated fat acids in the DM intramuscular fat content, was analyzed, its amount in comparison with normal animals was lower and much higher respectively. Also in comparison with normal animal was observed the high proportion of polar fatty acids and linoleic acids in Belgian blues (Smet et al., 2000). Animals with this phenotype besides increase production were better in feeding efficiency rather than their normal counterpart (Aenold et al., 2001).

Evaluation of mutation in myostatin and its role on regulation of muscles growth

Gene sequencing myostatin has been occurred in different species like cattle, sheep, chicken, goat and pig and in all of these species, this gene has three exons and two introns. There have been reports of nine mutations in coding regions of GDF-8 that cause various changes, of which three cause missense mutations, including two in exon 1 and one in exon 2. The six mutations, located in exons 2 and 3, result in premature stop codons, each of these mutations causes the negative effect of myostatin to stop the muscles growth and create double muscling phonotype (Belling et al., 2005).

Myostatin gene in bovine is located at the end of chromosome 2 and many mutations that cause appearance MM genotype and DM phonotype have been identified in this gene sequence. Mutations identified in cattle myostatin sequence are more than other species. (Riquetl et al., 1997)

sequencing GDF-8 gene in Belgian Blue breeds showed mutation which resulted in 11-bp deletion in coding region of myostatin cause stop decoding after amino acid 287 and it cause forming an inactive and incomplete protein so it stops the controlling role of myostatin protein on muscles growth then it appears DM phenotype. Mutation exon 3 in piedmontes breed changes nucleotide G into A and cysteine amino acid codon changes into tyrosine and probably inhibited myostatin gene function (McPherron and Lee, 1997).

In sheep, the myostatin gene is located on chromosome 2. For the first time muscular hypertrophy was found in Belgian Texel breed twenty single-nucleotide polymorphisms (SNPs) were identified in the region of GDF-8 in Texel sheep. Among There are, SNP g+6223G>A in the 3' untranslated region (3'UTR) that cause the body muscular (Clop et al., 2006). This SNP has been found in other breeds like Australian .New Zealand, Suffolk, Lincoln and Dorset horne, so g+6223G>A is used as an useful marker in crossing for improvement the sheep carcass traits (James et al., 2007).There is a significant association of g+6223.A allele with birth weight. A study done on Romney sheep in new Zealand showed average birth weight of sheep with g+6223 GG genotype is 5/8 kg whereas average birth weight of lambs with g+6223AG is 6/2 kg (Han et al., 2010)

Not only expression of myostatin gene is for skeletal muscles but there is mRNA in non-skeletal. Tissues like brain, heart muscle, purkinje fiber of the heart, mammary gland and some of white muscles. However the function of this mRNA has been remained unknown (ocamis et al., 2001).

Findings of study on muscular cells in chicken are quite different with others species and there is no significant difference between the level of mRNA myostatin in slow and fast muscles of chicken. In addition definite level of myostatin remains fixed during myoblast proliferation. The content of mRNA satellite cells differs with mature cells (Kobolak and Gocza, 2002).

Many mutation has been not observed at chicken myostatin gen. Studies conducted in breeds of chickens, have shown different mutations in the gene myostatin that cleared association of the myostatin gene with fat metabolism and body weight traits (Zhang et al., 2011)

In fish, amino acid sequence among different breeds show a high homology but and they differ from those of the higher vertebrates. In fish myostatin expression belongs not only to skeletal muscles but it has been in other tissues too, in brain, myostatin is expressed in optic lobe, cerebellum and hypothalamus. The ovarian form of the myostatin shows an increase in ovulating in fish different breed and it is expressed in red muscle of some breeds, these findings show that myostatin, in fish has a different role in comparison with higher vertebrates (Roberts and Goetz, 2001)

Studies have determined that depending on muscle type myostatin expression varies in different species. In rat myostatin protein level is high in fast muscles fibers than slow muscles (Sakuma et al., 2005). But mRNA and protein level in mouse is quite apposite of this fact (Carlson et al., 1999). Whereas mRNA and protein level in human muscular fibers are the same (Wehling et al., 2000).

Myostatin Role in meat production

In the meat industry, two traits, carcass quality and quantity of the most important factor affecting profit. These traits affect important factors such as genetics, nutrition, climate and so on. And is currently much research being done to predict carcass traits. Among the factors that determine the meat quality, genetic factor has a dominant role on meat quality (Kioumarsi et al., 2008).

Trend growing demand for lean meat with low levels of fat, which conformable with health standards scale, Results development of breeding programs and genetic improvement of commercial animals with higher production in last decades.

At recent years, there has been a wonderful progress on quantities and molecular genetics through mapping of the commercial animal’s genome and new opportunities have been provided for increase meat production and market for requirement consumers (Dekkers and Hospital, 2002). Different QLTs have been known that influence on muscles growth and carcass trait. At the present time few mutations in these QTLs have been identified and survey. The mutation in myostatin reported that has been associate with increase body weight and carcass trait in several species (Masri et al., 2011).

Mutated allele and inactive myostatin have a significant association with growth speed and carcass favorite traits. This allele causes increase muscles and low fat carcass. Farmers who raise calf carrying mutated allele of myostatin gain benefit more by production and market of meat (Casas et al., 2004).

Mutation in myostatin has an important effect on carcass quality and decreases amount of fatness in carcass .studies on south Devon cattle show that for each mutated allele there was 14.1 kg weight gain in animals carrying this allele compared with other animals (Wiener et al., 2009).

In animals with hypertrophy phonotype, fat amount cuts down into 50 percent and muscle mass increases 20 percent. Also connective tissues decrease in these animals so delicate and delicious meat is produced. It makes improves value of consumption a lot (McPherron et al., 1997).

Studies on Texel Dourest sheep shown that is a significant difference in carcass components between carriers of mutated allele with other animals. In animals with MM genotype traits such as live weight, carcass weight, muscle weight and its proportion to bone is significantly higher than normal animals and the amount of carcass fatness in animals carrying mutant allele is significantly lower than normal animals (Masri et al., 2011)

Other candidate genes effective on meat production

There are a lot of genes that influence on growth traits and carcass quality and can be as candidate genes for traits listed above or have be a close linkage with genes controlling these traits.

Calpastatin, leptin, growth hormone, prolactin, IGF and PIT are main genes that directly or with the effect on other hormones effect on meat quality and quantity (Saxena et al., 2009).

Based on studies about effective genes on meat production and association their polymorphism with, meat quality and quantative they are used as genetic markers in breeding plans for increase precise and selection-responsive.

Polymorphism myostatin genes in Iranian sheep

Survey diversity in local breeds very important for its survival because loss of genetic diversity in a breed cause increase in the rate of inbreeding and genetic abnormalities, thereby reduce animal performance, especially the reproductive traits (Mirhoseini et al., 2005).

Studies done on Iranian sheep show that polymorphism has not been observed for this gene; whereas European sheep have a high polymorphism of this gene. In Texel breed mutated allele of this gene has been fixed.

Study on karakul breed indicates that in 3exone of myostatin gene for wild allele are monomorphic (Zare, 2012). Study done in two breeds of Zell and Makoie were shown that the all of the animal are monomorphic and the mutant allele of the myostatin not found (Moradi, 2009). In another study done on Sanjabi breed less than three percent of samples had efficient allele in this gene and a low level of polymorphism was observed in this locus (Soufy et al., 2009).

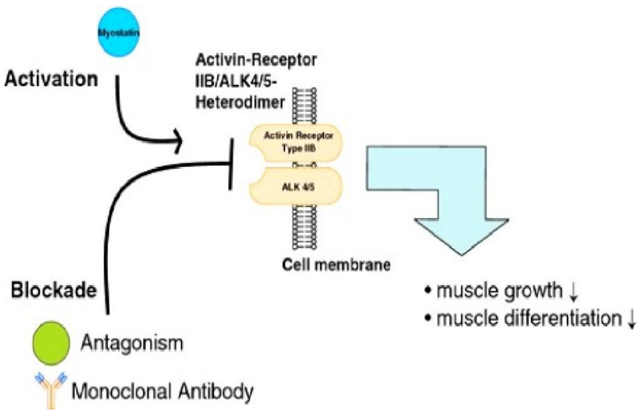

Figure 1. Myostatin pathway: myostatin levels regulate skeletal muscle cell


Figure 2. Belgian Blue cattle are "naturally" myostatin negative

In untranslatable region 3(3UTR), myostatin gene SNP 6223G→A has been known that increases muscle mass. In a study about three sheep breeds Zel, Chall and Zandi, this SNP has not been observed (Miar et al., 2009).

The magnitude and even the mode of action of the myostatin mutational effects on phenotype are probably affected by the genetic background of the breed in which the mutation is seen (Hahjipavlou et al., 2008).

Difference of myostatin polymorphism incidences between Iranian and European breeds comes back to selection plans for efficient allele of this gene. In European breeds the high improved selection of this allele has increased frequence of allele in commercial breeds and it has become fixed.

Restrictions myostatin gene in animal breeding

Myostatine gene is considered as the important locus in production traits. Several mutations on this gene cause double muscled phonotype and lead to massive muscle mass that one of the goal, raising the commercial animals. Select double muscled animals provide some problems such as dystocia. Animals with phenotype homozygote DM are affected more problems of dystocia rather than other animals even heterozygote type. Heterozygote animals with mutated allele somewhat have less danger of dystocia and they can produce homozygote calves for this allele so it is a simple solution to reduction of the costs and calves death probability. Double muscled phonotype lead to some other problems such as reduction fertility and increase of getting stressed and metabolically acidosis (Bellinge et al., 2005).

Conclusions

Identified mutations in sequences myostatin using molecular techniques is an effective solution for survey double muscle phenotype and help the breeders to get important information in order to make the precise decision for management and selecting the best population for reproduction and it lets the breeders have a lot of data about genetic status of myostatin gene in animals. Select right genotype with mutated allele is highly useful in crossed with beef breeds that produce fat and it causes protein and dry matter meat unchangeable. In order to determine genotype of myostatin and use of special programs for mating help to solve problems created by this gene application in breeding.

Corresponding Author:
Dr. Seyed Ziaeddin Mirhoseini
Department of Animal Science
University of Guilan, Rasht,
Rasht, Iran
E-mail:szmirhoseini@gmail.com; mirhosin@guilan.-ac.ir

References

1. Ghovvati S, Nassiri MR, Mirhoseini SZ, Moussavi AH, Javadmanesh A. Fraud identification in industrial meat products by multiplex PCR assay. Food Control 2009; 20**:** 696-699.
2. McPherron AC, Lee SJ. Double muscling in cattle due to mutations in the myostatin gene. Proceedings of the National Academy of Sciences 1997; 94**:**12457.
3. McPherron AC, Lawler AM, Lee SJ: Regulation of skeletal muscle mass in mice by a new TGF-superfamily member. Nature 1997;387**:**83-90.
4. Smith TPL, Lopez-Corrales NL, Kappes SM, Sonstegard TS: Myostatin maps to the interval containing the bovine mh locus. Mammalian Genome 1997; 8**:** 742-744.
5. Bellinge RHS, Liberles DA, Iaschi SPA, O'brien PA, Tay GK. Myostatin and its implications on animal breeding: a review. Animal Genetics 2005; 36**:**1-6.
6. Walling GA, Visscher PM, Wilson AD, McTeir BL, Simm G, Bishop SC. Mapping of quantitative trait loci for growth

and carcass traits in commercial sheep populations. Journal of Animal Science 2004;82: 2234-2245.

7. Clop A, Marcq F, Takeda H, Pirottin D, Tordoir X, Bibé B, Bouix J, Caiment F, Elsen JM, Eychenne F. A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. Nature Genetics 2006; 38:813-818.
8. Buenger L, Ott G, Varga L, Schlote W, Rehfeldt C, Renne U, Williams JL, Hill WG. Marker-assisted introgression of the Compact mutant myostatin allele MstnCmpt-dl1Abc into a mouse line with extreme growth effects on body composition and muscularity. Genetical Research 2004; 84:161-173.
9. Kobolak J, Gocza E. The role of the myostatin protein in meat quality-a review. Archiv Fur Tierzucht 2002;45: 159-170.
10. Gerrard DE, Thrasher KH, Grant AL, Lemenager RP, Judge MD. Serum-induced myoblast proliferation and gene expression during development of double muscled and normal cattle. Journal of Animal Science 1991; 69:317.
11. Smet S, Webb EC, Claeys E, Uytterhaegen L, Demeyer DI. Effect of dietary energy and protein levels on fatty acid composition of intramuscular fat in double-muscled Belgian Blue bulls. Meat Science 2000; 56: 73-79.
12. Arnold H, Della Fera MA, Baile CA. Review of myostatin history, physiology and applications. International Archives of Bioscience 2001; 1:1014-1022.
13. Riquetl I, Schoeberleinl A, Dunnerz S, Ménissier F, Massabanda I. A deletion in the bovine myostatin gene causes the double-muscled phenotype in cattle. Nature Genetics 1997; 17: 71.
14. James K, Russell MC, Janelle E, Hutton OV, Sang L. Evidence for multiple alleles effecting muscling and fatness at the Ovine GDF8 locus. 2007.
15. Han J, Zhou H, Forrest RH, Sedcole JR, Frampton CM, Hickford JGH: Effect of Myostatin (MSTN) g+ 6223G> A on Production and Carcass Traits in New Zealand Romney Sheep. Asian-Australasian Journal of Animal Sciences 2010, 23:863-866.
16. Kocamis H, McFarland DC, Killefer J. Temporal expression of growth factor genes during myogenesis of satellite cells derived from the biceps femoris and pectoralis major muscles of the chicken. Journal of Cellular Physiology 2001; 186:146-152.
17. Zhang G, Ding F, Wang J, Dai G, Xie K, Zhang L, Wang W, Zhou S. Polymorphism in Exons of the Myostatin Gene and Its Relationship with Body Weight Traits in the Bian Chicken. Biochemical Genetics 2011; 49:9-19.
18. Roberts SB, Goetz FW: Differential skeletal muscle expression of myostatin across teleost species, and the isolation of multiple myostatin isoforms. FEBS Letters 2001; 491: 212-216.
19. Sakuma K, Watanabe K, Sano M, Uramoto I, Totsuka T. Differential adaptation of GDF8/myostatin, FGF and leukemia inhibitory factor in overloaded, regenerating and denervated rat muscles. Biochemical et Biophysical Act 2005; 1497:77- 88.
20. Carlson CJ, Booth FW, Gordon SE: Skeletal muscle myostatin mRNA expression is fiber-type specific and increases during hindlimb unloading. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology 1999; 277: 601-606.
21. Wehling M, Cai B, Tidball JG: Modulation of myostatin expression during modified muscle use. The FASEB Journal 2000; 14:103-110.
22. Kioumarsi H, Jafari khorshidi K, Zahedifar M, Seidavi AR, Yahaya ZS, Rahman WA, Mirhosseini SZ. Estimation of relationships between components of carcass quality and quantity in Taleshi lambs. Asia Journal of Animal and Veterinary Advances 2008; 3:337-343.
23. Dekkers JCM, Hospital F. The use of molecular genetics in the improvement of agricultural populations. Nature Reviews Genetics 2002; 3: 22-32.
24. Masri AY, Lambe NR, Macfarlane JM, Brotherstone SH, W., Bünger L. Evaluating the effects of a single copy of a mutation in the myostatin gene (c.*1232 GNA) on carcass traits in crossbred lambs. Meat Science 2011; 87: 412-418.
25. Casas E, Bennett GL, Smith TPL, Cundiff LV. Association of myostatin on early calf mortality, growth, and carcass composition traits in crossbred cattle. Journal of Animal Science 2004; 82:2913-2918.
26. Wiener P, Woolliams JA, Frank-Lawale A, Ryan M, Richardson RI, Nute GR, Wood JD, Homer D, Williams JL. The effects of a mutation in the myostatin gene on meat and carcass quality. Meat Science 2009; 83:127-134.
27. Saxena VK, Sachdev AK, Gopal R, Pramod AB. Roles of important candidate genes on broiler meat quality. World's Poultry Science Journal 2009; 65: 37-50.
28. Mirhoseini SZ, Vahidie SMF, Gharehyazie B. Survey of efficiency of six microsatellite loci in Iranian indigenous cattle and buffalo populations. Iranian Journal of Biotechnology 2005, 3.
29. Zare J: Study on polymorphism of myostatin in Iranian Karakul sheep breed by PCR-RFLP marker. Ph.D. Thesis, Department of Animal Sciences, Faculty of Agriculture, Guilan University, Rasht- Iran, 2012
30. Moradi Shahr Baback H. Association polymorphism of calpastatin gene, myostatin, leptin and potassium genes with economic important trait, Blood metabolite and carcass traits in Persian Makoui, Lori-Bakhtiari and Zel sheep breed. Thesis, Department of Animal Sciences, Faculty of Agriculture, Tehran University. Tehran – Iran, 2009.
31. Soufy B, Mohammadabadi MR, Shojaeyan K, Baghizadeh A, Ferasaty S, Askari N, Dayani O. Evaluation of Myostatin Gene Polymorphism in Sanjabi Sheep by PCR-RFLP Method. Animal Science Journal of Tabriz University 2009; 19(1):81-89.
32. Miar Y, Salehi R, Aleyasi SA, Kolbehdari D, Raoofzadeh S. Polymorphisms in Myostatin Gene and its Association with Growth and Carcass Traits in Iranian Sheep. The 6 th National Biotechnology Congress of Iran, 2009.
33. Hadjipavlou G, Matika O, Clop A, Bishop SC. Two single nucleotide polymorphisms in the myostatin (GDF8) gene have significant association with muscle depth of commercial Charollais sheep. Animal Genetics 2008, 39: 346-353.

1/26/2012