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## REVIEW ARTICLE

### Applications of Myostatin in Poultry and Aquaculture - A Review

Ayoola John Shoyombo<sup>1</sup>, Yakubu Abdulmojeed<sup>2</sup>, Olubunmi Olayinka Alabi<sup>1</sup>, Mustapha Ayodele Popoola<sup>3</sup>, Ekemini Moses Okon<sup>1,\*</sup> and Damilare Olaniyi Arije<sup>1</sup>

<sup>1</sup>Department of Animal Science, College of Agricultural Sciences, Landmark University, P.M.B. 1001 Omu-Aran, Kwara State, Nigeria

<sup>2</sup>Department of Animal Science, Faculty of Agriculture, Nasarawa State University, Keffi, Shab-Lafia Campus, 950101, Lafia, Nigeria

<sup>3</sup>Research and Development, Office of the Executive Secretary, TETFUND, Nigeria

#### Abstract:

Polymorphism is an important component of animal genetic improvement. As a result, myostatin gene is largely involved in muscle formation and growth and is a great candidate gene for increased growth of muscle in animals. Myostatin negates the growth of muscle cells and is found across species. Literature shows various applications and importance of myostatin in poultry and aquaculture production. In poultry, variations in the myostatin gene have been linked to growth characteristics. In aquaculture, myostatin influences the enhancement of the muscle tissues of fish. Besides, myostatin plays a role in increasing the lipid content of muscle, lowering circulating glucose levels, and hepatosomatic index in fish. Studies on zebrafish as a model species have confirmed myostatin involvement in the muscle development of fish. Its expression is not limited to skeletal muscle but also occurs in the liver, brain, and other organs. In the myostatin-b-deficient zebrafish, the size of visceral adipose tissues shrank, and more lipids have been observed to accumulate in skeletal muscle than in wild-type fish. The inhibition or complete depletion of functional myostatin is known to cause the “double-muscled” in several cattle breeds and similar traits in other species. However, the “double-muscled” animals have captured the attention of breeders and researchers due to the enhanced muscular tissues; associated with productivity issues. For instance, the effect of myostatin inhibition has been associated with egg production. When compared to wild-type, myostatin homozygous mutant birds had a significantly delayed commencement of egg production in layers. It is therefore imperative to increase the knowledge of myostatin molecular genetics and bioactivity in various tissues in the poultry and aquaculture sector. This will enable improved productivity and enhanced contribution of animal-sourced proteins from both sectors of animal production.

**Keywords:** Polymorphism, Myostatin, Poultry, Aquaculture, Double muscle, Productivity.

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## 1. INTRODUCTION

Poultry is an essential source of food and revenue for farmers in many areas, both economically and socially. In many parts of the world, poultry has been an important source of dietary protein for the teeming global population. In the rural areas, poultry provides employment and social benefits ranging from the rearing of chicken, guinea fowl, etc. to their supply chain [1, 2]. Of these, food is the most important benefit from meats and eggs (for example chickens, ducks, and guinea fowl). Poultry is a more important source of protein than of calories with meat, eggs, and feathers. Over the years, the demand for livestock and their products has increased due to increased income, population, and urbanization across the world, particularly in developing countries [2, 3].

The widening gap between animal protein demand and

utilization in Nigeria calls for urgent investigation of resilient alternative livestock species as well as government policy changes that are supportive of sustainable poultry production. This is because poverty and climate change among other factors have impaired the successful use of improved conventional species of chickens and other livestock species to address poverty and hunger [4].

However, unconventional livestock holds a promising hope for farmers. Unconventional livestock species such as guinea fowls are reservoirs of valuable genetic resources, and many have traditionally been used as sources of animal protein. Being adapted to harsh environments with the ability to utilize natural resources more than conventional stocks cannot make it easy for landless and smallholder farmers to feed, manage and raise them. The continuing competition between commercial poultry and local poultry species in the Nigerian market boils down to one crucial factor: namely growth and maturity period. The continual quest for heavy breeds with more muscle mass per bird continues to implicate local poultry species demand

\* Address correspondence to this author at the Department of Animal Science, College of Agricultural Sciences, Landmark University, P.M.B. 1001 Omu-Aran, Kwara State, Nigeria;  
E-mails: [okon.ekemini@lmu.edu.ng](mailto:okon.ekemini@lmu.edu.ng); [okon.ekeminimoses@gmail.com](mailto:okon.ekeminimoses@gmail.com)

and consumption adversely despite their inherent adaptability advantage to the local climate. This issue continues to bedevil every aspect of poultry production as consumers' preferences will always determine the direction of research and production. Therefore, any focus of study to elevate the potential of indigenous poultry to compete with commercial stocks must center on this issue that commands consumer preference, namely growth. This review aims to consider one of such factors that greatly influence growth from the genetic angle.

Myostatin is a protein that prevents muscle growth. Two key aspects contribute to the popularity of myostatin. First and foremost, myostatin has a significant impact on muscle growth, implying a large potential for increased output. On the other hand, myostatin works as a negative regulator of muscle growth, causing muscle growth through enhanced cell division and/or hypertrophy when low amounts of the protein are present or when the protein is inactive.

According to Rodgers and Garikipati [5], the discovery of myostatin and the introduction of the "Mighty Mouse" sparked both scientific and applied research, as well as influenced popular culture. In mice and sheep, the inhibition of myostatin resulted in "double muscling," which has recently been reported in a child. Given the potential benefits of boosting muscle growth in agricultural and clinical settings, the rapid rise in the field is unsurprising. The importance of myostatin inhibition is also demonstrated in similar phenotypes of some domestic cattle breeds such as the Marchigiana, Piedmontese, and Belgian Blue due to the mutation of myostatin alleles [6, 7]. With the reasoning above, it goes to show the probable viability of developing indigenous local breeds from different poultry species in Nigeria using the myostatin nulling effect as a determinant.

According to literature, some avian species have had their myostatin genes cloned, including ducks, turkey, goose, quail, pigeon, and chicken [8]. Initial investigations with avian species and most non-mammalian vertebrates have attempted to link variations in myostatin expression to physiological responses to catabolic stress or important stages of skeletal muscle development. These results gave the initial demonstration that myostatin has the ability to inhibit growth activities in avian and fish skeletal muscle, albeit being predominantly descriptive.

Recent studies have investigated the functions of myostatin in different vertebrates with reference to polymorphism. In chickens, polymorphism of the myostatin gene has been connected to differences in body weight [9]. Also, Kim *et al.* [10] reported a minor but considerable positive effect on body weight and muscle mass in 3-day-old embryos due to immunoneutralization of myostatin. The study also indicated a lowered thigh and leg weights of post-hatch chickens administered polyclonal antibodies against Leucine Aminopeptidase (LAP) *in ovo*. The study provided the first functional proof that LAP suppresses the biological action of myostatin in a non-mammalian vertebrate.

The foregoing reports have proven that myostatin veritably as a genetic factor of growth is of key importance in elevating the potential of indigenous poultry species in Nigeria to

become competitive with commercial stocks while retaining their numerous fitness advantages.

### 1.1. Myostatin Editing and its Applications in Poultry

Myostatin (growth differentiation factor 8, GDF8) is a negative regulator predominantly expressed in skeletal muscle [11]. The treatment of myoblasts (muscle cells) with myostatin results in a reduction in proliferation and differentiation of the cells [12, 13].

The potential of myostatin inhibition to increase muscle mass in chickens and quail has generated attention in the poultry sector as a potential selection mechanism for increased meat production. The effect of myostatin inhibition has also been investigated on egg production to determine whether myostatin could be used in the layer industry to increase egg output. When compared to wild-type quail, myostatin homozygous mutant birds had a significantly delayed commencement of egg production in layers. The egg weight was also observed to be larger. However, during the active laying period, the number of eggs produced decreased [14].

The study by Zhang *et al.* [15] investigated the relationship between myostatin polymorphisms and production performance in chickens. The findings showed that variations in the myostatin gene are linked to chicken growth characteristics. Thus, the single nucleotide polymorphisms in the myostatin gene could serve as markers for marker-assisted selection in chicken breeding. The findings of Kim *et al.* [16] show a negative relationship between markers expression and pectoralis major muscle growth, laying the foundation for markers expression to be used as a selection marker for increased muscle growth in poultry.

Available literature has shown importance of myostatin in poultry. Myostatin gene is highly polymorphic in chicken and the mode of inheritance is possibly autosomal, monogenic, and partly recessive with incomplete penetrance [17, 18]. In chickens, Gu *et al.* [8] observed mutations in the regulatory areas of myostatin have been linked to abdominal fat percentage and weight, birth weight, breast muscle percentage, and weight.

Baron *et al.* [18], initiated exploration of myostatin in chickens during the study of the structure of the chicken myostatin gene. The study showed that the myostatin gene is similarly conserved with that of other vertebrates and is located in chromosome 7 with three exons and two introns (6693 bp in length) and produces about 375 latent amino acids. This finding was similarly reported in Bhattacharya *et al.* [19].

The study of Ye *et al.* [9] investigated the relationship between myostatin polymorphism and growth performance in broilers. The myostatin was reported as possessing pleiotropic effects on broiler performance. The result was associated with seven genetic variations in exon 1, three in exon 3, and three in intron 1 and 2. The primary role of myostatin was to regulate skeletal muscle growth. Ye *et al.* [9] further showed that the non-synonymous single nucleotide polymorphisms T4842G are linked to the alteration of an amino acid in the myostatin and may be connected to variation in body weight.

Also, Zhang *et al.* [20] showed that the exon 1 of the

myostatin in the Bian chicken breed reared for dual purposes in China possesses a 234G>A mutation. This has equally been reported in other Chinese chicken breeds (Arbor Acre, Jinghai, and Youxi) with four additional mutations in the 5'-regulatory region (A326G, C334G, C1346T, and G1375A). Single nucleotide polymorphisms in chicken myostatin were found to alter breast muscle weight and percentage, birth weight, abdominal fat weight and percentage, and adult weight in additional investigations on growth traits [20]. Three single nucleotide polymorphisms were identified by Gu *et al.* [21] in the 5' regulatory area and two single nucleotide polymorphisms in the 3' regulatory region. The single nucleotide polymorphisms varied in allele frequencies between breeds. The study further showed that homozygous genotypes AA and BB at a locus in the 5' regulatory region have a larger belly fat weight and percentage than the AB genotype in an F2 generation from a hybrid of broiler and silky chickens. In the DNA of Wenshang Luhua chicken, the upstream promoter region of myostatin was investigated. The findings showed that thirteen E-boxes were located upstream of myostatin, and the polymorphisms of E-boxes were examined for the first time [22]. Other studies on ducks looked into the relationship between myostatin polymorphisms and slaughter parameters like leg muscle weight and percentage, breast muscle percentage, and breast muscle weight. It was discovered that polymorphisms in the myostatin 5' regulatory region were linked to breast muscle percentage and rate of fat in the abdomen [23]. In addition, in a study of polymorphisms in Pekin ducks, Xu *et al.* [24] revealed three significant differences. The first is a T to C transition in the open reading frame (ORF) (position 129) that has been connected to the thickness of the breast muscle. The ORF for the T/C mutation had a second single nucleotide polymorphism at 708 bp, and the final 952TC had a strong association with the length of the "Fossilia Osis Mastodi", or dragon bone. According to Liu *et al.* [25], a transition of G>A at 2701bp in exon 3 of myostatin in Gaoyou ducks is linked to the rate of belly obesity. Six single nucleotide polymorphisms (g.106G>A, g.120A>G, g.159G>A, g.5368G>A, g.5389A>C, and g.5410G>A) were found in the first and third exons of the Sansui duck, with four loci appearing linked with leg dressing percentage, muscle percentage, and leg muscle weight [26].

In chickens, the connection between the expression of myostatin mRNA, body weight, muscle mass, and growth rate is not well understood. In view of this, Duo *et al.* [27] investigated this relationship and found that myostatin expression is linked to muscle development regulation and body growth, with two distinct regulatory mechanisms switching between days 30 and 60.

Different polymorphisms in the myostatin gene have been investigated in different poultry breeds. Zhang *et al.* [20] observed polymorphisms on myostatin in Youxi, Jinghai, and Bian breeds. Liu *et al.* [24], Xu *et al.* [25], and Zhao *et al.* [26], investigated polymorphisms on myostatin across different positions in Sansui duck, Gaoyou duck, and Pekin duck, respectively.

From the foregoing reports, it illustrates the extent of work done on the myostatin gene in poultry breeds from other climes

and most of these reports points to the feasibility of using this gene in breeding to boost productivity in the sector [27]. In Nigeria, Fijabi *et al.* [28] reported a study of polymorphism in the myostatin gene and its relationship to body weight in Nigeria indigenous Turkey. The findings showed that three allelic variants, A, B, and C, were discovered with frequencies of 0.79, 0.20, and 0.01, respectively, while three genotypes, AA, AB, and AC, were controlled with frequencies of 0.58, 0.40, and 0.02, respectively. The likelihood ratio (G2; 0.145757) and chi-square test (X2; 0.342138) probabilities for Hardy-Weinberg equilibrium show that the sampled population was in equilibrium. In the population, the observed heterozygosity, Shannon information index, number of effective alleles, and Nei's gene diversity indices were 0.4200, 0.5542, 1.5056, and 0.3358, respectively, indicating moderate to high diversity. At 4, 8, and 12 weeks of age, there was no significant ( $P > 0.05$ ) link between body weight and genotype. The polymorphism nature of the myostatin gene allows for genetic enhancement through selective breeding. Although, its polymorphic variations have little effect on body weight in Nigerian indigenous turkeys.

Since time immemorial, the attention of poultry farmers in Nigeria has been integrally focused on chicken with minimal attention paid to other poultry species. The many underrated, but highly promising poultry species such as turkey, quail, and guinea fowl have been left unexplored and underutilized, hence this review is to point out the benefits of studies on myostatin gene in Nigeria poultry species and expose the critical neglect that is ongoing with regards to this species in terms of utilizing their genetic potential to improve poultry production in Nigeria.

## 1.2. Myostatin Editing and its Applications in the Aquaculture Sector

Aquaculture plays an important role in meeting the increasing demand for animal-source foods. With the current global population and projection of over nine billion by 2050, aquaculture will become the major supplier of animal protein for human utilization [29, 30]. In the past few decades, aquaculture has seen tremendous expansion in terms of production volume and value; matched with an increased demand for aquaculture products, particularly fish [31]. This expansion can be attributed to the depletion of wild fishery stock, international trade and a rising global human population that has resulted in the significant increase in demand for aquatic animal-source foods [32, 33] (Ottinger *et al.*, 2016; Sprague *et al.*, 2016). The success of the aquaculture sector, along with a reduction in global fisheries output, has substantially increased the importance of the aquaculture sector for human nutrition and sustenance [34].

In developing countries, the incapability of aquaculture farms to minimize production costs has been a fundamental constraint despite the steady growth of aquaculture across the world. This limitation further incapacitates aquaculture farmers to supply their products at a market price that is quite competitive [35]. Initially, research and development resources in advancing aquaculture focused on optimizing feed composition as well as enhancing the culturing processes.

Although research and development in these areas have resulted in innovative and sustainable approaches to cultural practices, the average per unit productivity seems unchanged across many industries utilizing these approaches [36]. In view of this, the adoption of genetic technologies seems to be the only way forward towards achieving significant increases in aquaculture productivity. In particular, genetic technologies stand the chance to considerably improve the productivity of aquaculture species, of which an optimal culture technique has been established [36 - 38].

Depending on the culture species, many desirable traits have been singled out to boost aquaculture productivity and eventually increase its profitability. Specifically, among the many desirable traits, the growth rate of the cultured species has usually been the most significant of these traits [39]. This is because the growth rate is central for an animal to attain a harvest size within a shorter time frame, hence, shortening the production cycle, minimizing production costs, and maximizing profits [40].

Over the years, improved growth rates to attain shorter harvest times have become very important in aquaculture operations, where costs and risk of a disease outbreak are generally higher compared to livestock production systems [36]. Such dramatic improvement in the performance of cultured species in the aquaculture sector has been one of the single factors behind the expansion and profitability of the industry. This has been attributed to the use of various genetic technologies to improve growth as obtained in terrestrial livestock industries such as swine, cattle, swine, and poultry [41, 42].

Among the many targeted traits, growth has typically been the most essential and desired trait to increase aquaculture farm production and profitability [39, 40]. Over the years, the growth rate of various species of aquatic organisms has been improved through research and the application of several genetic techniques. These include the use of stocks of single, fast-growing sex (*i.e.*, all-male tilapia) and utilization of chromosomal modification to produce enhanced stock with an extra set of chromosomes (*i.e.*, triploids). Other genetic techniques of importance include selective breeding systems, which select and match fast-growing individuals to produce better offspring, and genetic modification of growth-related genes [43 - 46].

Among these genetic techniques, the application of the single-gene strategy has lately acquired a high preference among aquaculture researchers to boost productivity. Although these strategies have shown highly positive outcomes in terms of improvement of production in select species, their widespread adoption is still constrained by some factors such as limited technological facilities, government regulation, and public acceptance [36, 47, 48]. Above all, many aquaculture species are still not capable of being efficiently bred in captivity and this is a clear limitation to the majority of the above-mentioned techniques. It is expected that such limitations might persist when additional aquaculture species are domesticated. As a result, it is imperative that a growth strategy that is less dependent on the reproductive cycle remains one of the favourable options for advancing

aquaculture production and profitability on a commercial scale [49].

The use of a single gene strategy has accelerated the characterisation and investigation of a number of potential genes with large effects on growth, one of which is myostatin. Several studies have found that genes identical to the myostatin gene found in cattle are found throughout the animal kingdom and that many species have a substantial relationship with growth functions [50]. Therefore, myostatin is a particularly attractive candidate gene for improving aquaculture production due to its essential function in the regulation of growth [36].

At the moment and in the near future, aquaculture stands to benefit tremendously from breakthroughs through genetic technologies targeting growth genes such as myostatin. These technologies are capable of being adapted to target growth genes, particularly in fish to boost production yield [51, 52]. In view of this, it is critical to characterize and understand genes that have a significant impact on growth. Thus, the myostatin gene is one such gene that has the ability to not only boost the growth of aquaculture species such as fish but improve productivity in the long run.

### **1.3. Myostatin Editing and its Application for Enhancing Muscle Growth in Aquaculture**

In recent years, several genetic techniques have been researched and utilized to improve the growth rate of aquatic species [53]. The use of genetic editing tools like TALENs, CRISPR/Cas9, and transgenic technology has helped researchers learn more about somatic growth modulation in fish [54, 55]. Myostatin produced from a precursor protein in teleost fish contains a signal peptide, an N-terminal prodomain, and a C-terminal active domain, similar to myostatin in other vertebrate species [56]. The deletion of myostatin or its inhibition in mammals has been shown to increase muscle mass significantly (*e.g.*, double-muscling cattle) through hypertrophy, hyperplasia, or a combination of both [57]. Despite a remarkable degree of conservation with the mammalian protein, the precise function of myostatin in fish remains unknown [58]. In contrast to mammalian species, which have only one copy of myostatin, certain fish species contain numerous isoforms with distinct patterns of expression [59, 60]. Many species of fish use hyperplasia to prolong muscle growth throughout their lives [36]. Thus, the possibility of lowering or blocking the function of this gene/protein has been the primary focus of research efforts. This focus has been aimed at enhancing fish growth *via* a variety of biotechnological ways as obtained in mammals [61, 62].

In mammals, the deactivation or reduction of myostatin causes a considerable muscle mass increase to occur, a condition known as “double muscling” [63]. In livestock production, “double muscling” intensely increases the muscular mass and consequently improves economic benefits [64]. As part of an attempt to discover approaches to reduce myostatin in fish and similarly enhance economic benefits, Rebhan and Funkenstein [65] investigated the production and purification of two possible binding proteins to fish myostatin leading to increased muscle growth. The two binding proteins to fish myostatin: follistatin and myostatin prodomain were

both cloned from the marine species gilthead sea bream, *Sparus aurata*. The findings of Rebhan and Funkenstein [65] provided a method for reducing bioactive myostatin and, as a result, enhancing muscle growth in aquaculture fish.

In other investigations, Gao *et al.* [66] reported that myostatin-b-deficient zebrafish had larger circumferences and body weights than the wild-type sibling control fish starting at the adult stage (80 days postfertilization). According to a study by Xu *et al.* [56], muscle mass accounts for a greater proportion of body mass in fish than in mammals. In view of this, the findings of Gao *et al.* [66] established that the increased muscle growth in Zebrafish was associated with an increase in body weight, which could be a result of altered somatic metabolism caused by myostatin-b deficiency. Studies that used other species, specifically zebrafish, have confirmed myostatin involvement in the muscle development of fish. Xu *et al.* [56] reported that a transgenic strain of zebrafish that overexpresses the myostatin prodomain under a muscle-specific promoter (an inhibitor of myostatin activity) showed an increase in the number of myofibers without a significant change in fiber size. Hence, resembling the hyperplasia seen in cattle double-muscle breeds with myostatin gene inactivating mutations. As obtained in mammals, myostatin is proteolytically processed and secreted in zebrafish, and it has been confirmed in other fish that its expression is not limited to skeletal muscle but also occurs in the liver, brain, and other organs [59, 67].

Zhong *et al.* [68] used the CRISPR/Cas9 technique to modify the myostatin gene and found significantly more muscle cell growth in *mstnba* mutated common carp (*Cyprinus carpio*). Similarly, Khalil *et al.* [69] (2017) utilized the CRISPR/Cas9 technique through zygote injection to target myostatin in the channel catfish, *Ictalurus punctatus*. The study shows that myostatin-edited fry had significantly more muscle cells than controls, and their mean body weight increased by 29.7%. The findings revealed that CRISPR/Cas9 can be successfully employed to target the myostatin gene to produce growth-enhanced fish and increase productivity. Furthermore, Sun *et al.* [68 - 70] employed CRISPR/Cas9 to develop more prominent growth characteristics in blunt snout bream. The myostatin-deficient (*mstna* and *mstnb* target) fish had a significantly larger average muscle fiber size and other growth parameters than the control fish.

#### 1.4. Myostatin Editing and its Application in Regulating Fat Mass in Aquaculture

Besides muscle growth, several previous studies have found that myostatin is not just essential in myogenesis (differentiation of myoblast into a muscle cell) but also in adipogenesis (development and accumulation of fat-laden cells as adipose tissue) [64, 71, 72]. The precise role of myostatin in adipogenesis is debatable at the moment [55]. However, two separate roles are attributed to myostatin relative to lipogenesis: inhibiting [73] and promoting lipogenesis [74].

Myostatin has the capacity to prevent myogenic differentiation. It can also increase the differentiation of mesenchymal cells into adipogenic lineages [74]. Myostatin has also been shown to mostly inhibit adipogenesis in

preadipocytes but enhance adipogenesis in pluripotent stem cells [64] (Deng *et al.*, 2017). In mice, the inhibition and deletion of myostatin primarily result in increased muscle mass and decreased fat mass [73]. When myostatin is inhibited in mammalian muscle, the fat mass is observed to reduce but not in adipose tissue. However, when myostatin levels become overexpressed in the adipose tissue, the metabolic rate is boosted and this protects against diet-induced obesity [71].

The inhibition of myostatin has been studied in animals and has been linked to a reduction in fat tissue. Zhao *et al.* [75] observed that when myostatin was repressed in transgenic mice using a propeptide cDNA sequence, fat masses in the retroperitoneal, epididymal, and subcutaneous areas were drastically reduced compared to wild type mice. Similarly, Mosler *et al.* [76] showed that knocking down myostatin with siRNA reduced visceral fat in adult mice. McPherron *et al.* [77] revealed that myostatin may be more effective in lowering adipose weight growth rather than inducing weight reduction. Furthermore, Dong *et al.* [78] reported that when myostatin is blocked by an anti-myostatin peptide, white adipose tissue is converted to brown adipose tissue. Also, energy expenditure and fatty acid oxidation are enhanced in high fibre diet-fed mice.

From the above, it is well established that myostatin plays a vital role in lipid metabolism and adipogenesis in mammals, but its function in fishes has not been completely investigated [69, 79]. In view of the above, Galt *et al.* [79] investigated the relationship between dietary lipid levels and myostatin expression in rainbow trout (*Oncorhynchus mykiss*). When compared to a low-fat diet (10% lipid), a five-week high-fat diet (25% lipid) intake increased the white muscle lipid content and lowered circulating glucose levels and hepatosomatic index. In addition, the high-fat diet (25% lipid) reduced the expression of myostatin-1a and myostatin-1b in white muscle and myostatin-1b in the brain tissue of the fish. Thus, myostatin plays an essential role in lipid utilization and muscle metabolism in fish.

Xu *et al.* [56] used quantitative PCR to evaluate the expression of key genes in muscle tissue in an attempt to investigate the mechanism of the energy metabolism features in the myostatin-b-deficient fish. The expression levels of genes involved in lipolysis, lipogenesis, and gluconeogenesis were higher in the myostatin-b-deficient zebrafish, but those involved in branched amino acid degradation were lower. This finding further revealed that lipid metabolism became highly stimulated, implying that lipids provided more energy to myostatin-b-deficient zebrafish muscle tissue.

In numerous animal species, depletion of myostatin resulted in increased muscle growth. However, the report on the complete depletion of myostatin in teleost fish has not yet been reported except few studies [66, 80, 81]. Gao *et al.* [66], investigated two distinct myostatin-b-deficient mutant lines in zebrafish. Although the total lipid/body weight ratios of the myostatin-b-deficient zebrafish and the control fish were identical, the distribution of lipids was different. In the myostatin-b-deficient zebrafish, the size of visceral adipose tissues shrank, and more lipids accumulated in skeletal muscle than in wild-type control fish. Based on the transcriptional

expression profiles, Gao *et al.* [66] further showed that lipid metabolism, including lipolysis and lipogenesis processes, was greatly active in myostatin-b-deficient zebrafish, indicating that energy metabolism in myostatin-b-deficient zebrafish shifted from protein-dependent to lipid-dependent. Ohama *et al.* [81] conducted a feeding trial on red sea bream (*Pagrus major*) after complete myostatin (*Pm-mstn*) knockout using CRISPR/Cas9. The myostatin complete knockout fish had a better somatic growth rate, feed efficiency, weight gain, and a higher ability to accumulate ingested protein than wild-type fish.

### 1.5. Myostatin and Future Implications in the Poultry and Aquaculture sector

According to some researchers, myostatin mutations are the primary cause of hypertrophy, with other gene changes playing a minor impact [82]. MSTN inactivation has thus been offered as a technique for boosting food animal muscle growth and treating human disorders involving muscular weakness and dystrophy [83]. The most obvious biological benefit of altering myostatin function is to improve muscle development while, in most cases, inhibiting intra-muscular fat deposition. Due to the indirect effect of neutralizing myostatin's activities on adiposity, these technologies may be effective in the treatment of obesity and type 2 diabetes. A marketing campaign promising "more muscle, less fat" is appealing and one that these technologies may potentially provide. As biological breakthroughs become more widely known, inhibiting myostatin's functions for cosmetic goals is becoming more likely, if not inevitable [5]. Also, the need for comparative modeling and analysis of myostatin gene action in each poultry specie and other farm animals is recommended to enable more accurate data on which breeding and production may be based and eliminate as much as possible unwitting dangers as a result of nulling myostatin gene in Nigeria poultry species, also according to Rodgers and Garikipati [5]. The underlying mechanisms involved in nulling or not nulling of myostatin gene and its actions present a once-in-a-lifetime opportunity to test duplication-degeneration-complementation *vs.* conflicting evolutionary models—double-recessive that could explain the molecular basis of fundamental evolutionary processes. There is a low understanding of how perceptibly modest alterations in the gene affect structure and function. This might dramatically affect phenotypic differences across species and/or speciation itself. As a result, increasing knowledge of myostatin molecular genetics and bioactivity in various tissues and creatures has the potential to impact both research and society.

The concept stated above recommends a strategy of dual myostatin and activin opposition to enhancing tissue growth in the meat production sector, for which the focus is on muscle growth. Interestingly, this could be accomplished by using a combination of compounds that specifically inhibit myostatin and activin activity or a single protein that works at a signalling convergence point at the receptor level *via* a ligand trap or blocking antibody [84, 85].

### CONCLUSION

Polymorphism may be observed in nearly all livestock species, including poultry, and it can be seen at all levels of genetic organization, from DNA sequence to significant

physical features. In poultry and aquaculture production, genetic polymorphism adds to the phenotype diversity. Besides, it is an important component of animal genetic improvement. This genetic variation has generated great interest in researchers in both sectors of animal production for increased meat production. As a result, the myostatin gene is largely involved in muscle formation and growth and has been a great candidate gene for increased muscle growth in animals.

In poultry and aquaculture production, myostatin inhibition enhanced muscle growth in chicken and fish to boost production in commercial poultry and aquaculture industries. Such a boost has the potential to improve the growth of the industry by enabling farmers to grow larger chicken and fish without increasing the amount of feed consumption. One of the benefits of this strategy is that the modified genes introduced into the chicken or fish employ the same mechanism in livestock animals such as cattle. Thus, myostatin is an important target gene for poultry and aquaculture research to boost productivity.

### LIST OF ABBREVIATION

LAP = Leucine Aminopeptidase

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### REFERENCES

- [1] Shamsuddoha M, Quaddus M, Klass D. Sustainable poultry production process to mitigate socio-economic challenge. *Humanomics* 2015; 31(3): 242-59. [http://dx.doi.org/10.1108/H-09-2012-0017]
- [2] Aswani PB, Lichoti JK, Masanga J, *et al.* Characterisation of the phenotypes associated with body growth and egg production in local chickens from three agro-climatic zones of Kenya. *Livest Res Rural Dev* 2017; 29(32): 1-10. http://www.lrrd.org/lrrd29/2/aswa29032.htm
- [3] Yitbarek MB. Livestock and livestock product trends by 2050. *IJAR* 2019; 4: 30.
- [4] Committee on Considerations for the Future of Animal Science Research, Science and Technology for Sustainability Program, Policy and Global Affairs, Board on Agriculture and Natural Resources, Division on Earth and Life Sciences, & National Research Council. *Critical Role of Animal Science Research in Food Security and Sustainability*. US: National Academies Press 2015.
- [5] Rodgers BD, Garikipati DK. Clinical, agricultural, and evolutionary biology of myostatin: a comparative review. *Endocr Rev* 2008; 29(5): 513-34. [http://dx.doi.org/10.1210/er.2008-0003] [PMID: 18591260]
- [6] Kambadur R, Sharma M, Smith TPL, Bass JJ. Mutations in myostatin (GDF8) in double-muscled Belgian Blue and Piedmontese cattle. *Genome Res* 1997; 7(9): 910-5. [http://dx.doi.org/10.1101/gr.7.9.910] [PMID: 9314496]
- [7] Page AL, Parsot C. Chaperones of the type III secretion pathway: jacks of all trades. *Mol Microbiol* 2002; 46(1): 1-11.

- [http://dx.doi.org/10.1046/j.1365-2958.2002.03138.x] [PMID: 12366826]
- [8] Gu Z, Zhang Y, Shi P, Zhang YP, Zhu D, Li H. Comparison of avian myostatin genes. *Anim Genet* 2004; 35(6): 470-2. [http://dx.doi.org/10.1111/j.1365-2052.2004.01194.x] [PMID: 15566475]
- [9] Ye X, Brown SR, Nones K, Coutinho LL, Dekkers JCM, Lamont SJ. Associations of myostatin gene polymorphisms with performance and mortality traits in broiler chickens. *Genet Sel Evol* 2007; 39(1): 73-89. [http://dx.doi.org/10.1186/1297-9686-39-1-73] [PMID: 17212949]
- [10] Kim YS, Bobbili NK, Paek KS, Jin HJ. Production of a monoclonal anti-myostatin antibody and the effects of in ovo administration of the antibody on posthatch broiler growth and muscle mass. *Poult Sci* 2006; 85(6): 1062-71. [http://dx.doi.org/10.1093/ps/85.6.1062] [PMID: 16776476]
- [11] McPherron AC, Lawler AM, Lee SJ. Regulation of skeletal muscle mass in mice by a new TGF- $\beta$  superfamily member. *Nature* 1997; 387(6628): 83-90. [http://dx.doi.org/10.1038/387083a0] [PMID: 9139826]
- [12] Sancho Muñoz A, Guitart M, Rodríguez D, Gea J, Martínez Llorens J, Barreiro Portela E. Increased myostatin as a negative regulator of muscle regeneration potential in sarcopenic COPD patients: clinical implications. *Eur Respir J* 2020; 56: 4659. [http://dx.doi.org/10.1183/13993003.congress-2020.4659]
- [13] Suh J, Lee YS. Myostatin inhibitors: Panacea or predicament for musculoskeletal disorders? *J Bone Metab* 2020; 27(3): 151-65. [http://dx.doi.org/10.11005/jbm.2020.27.3.151] [PMID: 32911580]
- [14] Lee J, Kim DH, Brower AM, Schlachter I, Lee K. Effects of myostatin mutation on onset of laying, egg production, fertility, and hatchability. *Animals (Basel)* 2021; 11(7): 1935. [http://dx.doi.org/10.3390/ani11071935] [PMID: 34209534]
- [15] Zhang X X, Ran J S, Lian T, *et al.* The single nucleotide polymorphisms of myostatin gene and their associations with growth and carcass traits in Daheng broiler. *Brazilian J Poul Sci* 2019; 21
- [16] Kim DH, Choi YM, Suh Y, *et al.* Research Note: Association of temporal expression of myostatin with hypertrophic muscle growth in different Japanese quail lines. *Poult Sci* 2020; 99(6): 2926-30. [http://dx.doi.org/10.1016/j.psj.2019.12.069] [PMID: 32475426]
- [17] Ménéssier F. General survey of the effect of double muscling on cattle performance. Muscle hypertrophy of genetic origin and its use to improve beef production. Dordrecht: Springer 1982; pp. 23-53. [http://dx.doi.org/10.1007/978-94-009-7550-7\_2]
- [18] Baron EE, Wenceslau AA, Alvares LE, Nones K, Ruy DC, Schmidt GS, *et al.* High level of polymorphism in the myostatin chicken gene. *Proc 7th World Congr Genet Appl Livest Prod Montpellier* 2002; 19-23.
- [19] Bhattacharya TK, Chatterjee RN, Dushyanth K, Shukla R. Cloning, characterization and expression of myostatin (growth differentiating factor-8) gene in broiler and layer chicken (*Gallus gallus*). *Mol Biol Rep* 2015; 42(2): 319-27. [http://dx.doi.org/10.1007/s11033-014-3753-x] [PMID: 25479731]
- [20] Zhang GX, Zhao XH, Wang JY, Ding FX, Zhang L. Effect of an exon 1 mutation in the myostatin gene on the growth traits of the Bian chicken. *Anim Genet* 2012; 43(4): 458-9. [http://dx.doi.org/10.1111/j.1365-2052.2011.02274.x] [PMID: 22497311]
- [21] Gu Z, Dahai Z, Ning L, Hui L, Xuemei D, Changxin W. The single nucleotide polymorphisms of the chicken myostatin gene are associated with skeletal muscle and adipose growth. *Sci China C Life Sci* 2004; 47(1): 25-30. [http://dx.doi.org/10.1360/02yc0201] [PMID: 15382673]
- [22] Hu W, Chen S, Zhang R, Lin Y. Single nucleotide polymorphisms in the upstream regulatory region alter the expression of myostatin. *In Vitro Cell Dev Biol Anim* 2013; 49(6): 417-23. [http://dx.doi.org/10.1007/s11626-013-9621-5] [PMID: 23670598]
- [23] Junqing L, Shuisheng H, Wei H, Junying Y, Wenwu W. Polymorphisms in the myostatin gene and their association with growth and carcass traits in duck. *Afr J Biotechnol* 2011; 10(54): 11309-12. [http://dx.doi.org/10.5897/AJB11.512]
- [24] Xu TS, Gu LH, Zhang XH, *et al.* IGF-1 and FoxO3 expression profiles and developmental differences of breast and leg muscle in pekin ducks (*Anas platyrhynchos domestica*) during postnatal stages. *J Anim Vet Adv* 2013; 12(7): 852-8.
- [25] Liu Q, Chen YH, Cai FX, Zhu WQ, Wang ZY, Zhang TJ. Polymorphisms in exon 3 of MSTN gene and its relationship with abdominal fat rate in Gaoyou duck. *China Poult* 2012; 34: 24-30.
- [26] Zhao ZH, Li H, Yi HJ, Peng BX. The Correlation Between Polymorphisms of the MSTN Gene and Slaughter Traits in Sansui Ducks. *Pak J Zool* 2016; 48(5): 201817603.
- [27] Tait-Burkard C, Doeschl-Wilson A, McGrew MJ, *et al.* Livestock 2.0 – genome editing for fitter, healthier, and more productive farmed animals. *Genome Biol* 2018; 19(1): 204. [http://dx.doi.org/10.1186/s13059-018-1583-1] [PMID: 29301551]
- [28] Fijabi OE, Osaiyuru OH, Akinyemi MO, *et al.* Myostatin gene polymorphism and its association with body weight in Nigerian indigenous turkey. *Thai J Agric Sci* 2020; 53(2): 58-66.
- [29] Dauda AB, Natrah I, Karim M, Kamarudin MS, Bichi AH. African catfish aquaculture in Malaysia and Nigeria: Status, trends and prospects. *Fish Aquac J* 2018; 9(1): 1-5. [http://dx.doi.org/10.4172/2150-3508.1000237]
- [30] Food and Agriculture Organization. Sustainability in action. Rome: State of World Fisheries and Aquaculture 2020; p. 200.
- [31] FAO. The State of World Fisheries and Aquaculture 2018 - Meeting the sustainable development goals. Rome: Licence: CC BY-NC-SA 3.0 IGO 2018.
- [32] Ottinger M, Clauss K, Kuenzer C. Aquaculture: Relevance, distribution, impacts and spatial assessments – A review. *Ocean Coast Manage* 2016; 119: 244-66. [http://dx.doi.org/10.1016/j.ocecoaman.2015.10.015]
- [33] Sprague M, Dick JR, Tocher DR. Impact of sustainable feeds on omega-3 long-chain fatty acid levels in farmed Atlantic salmon, 2006–2015. *Sci Rep* 2016; 6(1): 21892. [http://dx.doi.org/10.1038/srep21892] [PMID: 26899924]
- [34] FAO (2009) Statistics and Information Service of the Fisheries and Aquaculture Department/Service FAO yearbook Fishery and Aquaculture Statistics 2009/FAO annuaire. Rome: FAO 2011.
- [35] Kumar P, Jain KK, MunilKumar S, Sudhagar SA. Alternate feeding strategies for optimum nutrient utilization and reducing feed cost for semi-intensive practices in aquaculture system-A review. *Agric Rev (Karnal)* 2017; 38(2): 145-51. [http://dx.doi.org/10.18805/ag.v38i02.7946]
- [36] De Santis C. Regulation of growth: understanding the myostatin functioning in two important aquaculture species, barramundi (*Lates calcarifer*) and black tiger shrimp (*Penaeus monodon*). (Doctoral dissertation, James Cook University) 2011.
- [37] Bossier P, Ekasari J. Biofloc technology application in aquaculture to support sustainable development goals. *Microb Biotechnol* 2017; 10(5): 1012-6. [http://dx.doi.org/10.1111/1751-7915.12836] [PMID: 28941177]
- [38] Adewale Omole I. Biotechnology as an important tool for improving fish productivity. *American J Biosci Bioeng* 2017; 5(1): 17. [http://dx.doi.org/10.11648/j.bio.20170501.14]
- [39] Gjedrem & Akvaforsk. Selection and breeding programs in aquaculture. Gjedrem T, Ed. New York: Springer 2005; 2005: p. 360.
- [40] Ye B, Wan Z, Wang L, *et al.* Heritability of growth traits in the Asian seabass (*Lates calcarifer*). *Aquac Fish* 2017; 2(3): 112-8. [http://dx.doi.org/10.1016/j.aaf.2017.06.001]
- [41] Georges M, Charlier C, Hayes B. Harnessing genomic information for livestock improvement. *Nat Rev Genet* 2019; 20(3): 135-56. [http://dx.doi.org/10.1038/s41576-018-0082-2] [PMID: 30514919]
- [42] Houston RD, Bean TP, Macqueen DJ, *et al.* Harnessing genomics to fast-track genetic improvement in aquaculture. *Nat Rev Genet* 2020; 21(7): 389-409. [http://dx.doi.org/10.1038/s41576-020-0227-y] [PMID: 32300217]
- [43] Du SJ, Gong ZY, Fletcher GL, *et al.* Growth enhancement in transgenic Atlantic salmon by the use of an “all fish” chimeric growth hormone gene construct. *Biotechnology (N Y)* 1992; 10(2): 176-81. [PMID: 1368229]
- [44] Gjøen H, Bentsen HB. Past, present, and future of genetic improvement in salmon aquaculture. *ICES J Mar Sci* 1997; 54(6): 1009-14. [http://dx.doi.org/10.1016/S1054-3139(97)80005-7]
- [45] Mair GC, Abucay JS, Abella TA, Beardmore JA, Skibinski DOF. Genetic manipulation of sex ratio for the large-scale production of all-male tilapia *Oreochromis niloticus*. *Can J Fish Aquat Sci* 1997; 54(2): 396-404. [http://dx.doi.org/10.1139/f96-282]
- [46] Liu JL, Coschigano KT, Robertson K, *et al.* Disruption of growth hormone receptor gene causes diminished pancreatic islet size and increased insulin sensitivity in mice. *Am J Physiol Endocrinol Metab* 2004; 287(3): E405-13. [http://dx.doi.org/10.1152/ajpendo.00423.2003] [PMID: 15138153]
- [47] Ma X, Mau M, Sharbel TF. Genome editing for global food security.

- Trends Biotechnol 2018; 36(2): 123-7.  
[http://dx.doi.org/10.1016/j.tibtech.2017.08.004] [PMID: 28893405]
- [48] Betanzo-Torres EA, Piñar-Álvarez MÁ, Sandoval-Herazo LC, Molina-Navarro A, Rodríguez-Montoro I, González-Moreno RH. Factors That Limit the Adoption of Biofloc Technology in Aquaculture Production in Mexico. *Water* 2020; 12(10): 2775.  
[http://dx.doi.org/10.3390/w12102775]
- [49] Regan T, Bean TP, Ellis T, et al. Genetic improvement technologies to support the sustainable growth of UK aquaculture. *Rev Aquacult* 2021; 13(4): 1958-85.  
[http://dx.doi.org/10.1111/raq.12553]
- [50] Grade CVC, Mantovani CS, Alvares LE. Myostatin gene promoter: structure, conservation and importance as a target for muscle modulation. *J Anim Sci Biotechnol* 2019; 10(1): 32.  
[http://dx.doi.org/10.1186/s40104-019-0338-5] [PMID: 31044074]
- [51] Thomas M, Langley B, Berry C, et al. Myostatin, a negative regulator of muscle growth, functions by inhibiting myoblast proliferation. *J Biol Chem* 2000; 275(51): 40235-43.  
[http://dx.doi.org/10.1074/jbc.M004356200] [PMID: 10976104]
- [52] Yang Z, Yu Y, Tay YX, Yue GH. Genome editing and its applications in genetic improvement in aquaculture. *Rev Aquacult* 2021; 1-13.
- [53] Osmond ATY, Colombo SM. The future of genetic engineering to provide essential dietary nutrients and improve growth performance in aquaculture: Advantages and challenges. *J World Aquacult Soc* 2019; 50(3): 490-509.  
[http://dx.doi.org/10.1111/jwas.12595]
- [54] Barman HK, Rasal KD, Chakrapani V, et al. Gene editing tools: state-of-the-art and the road ahead for the model and non-model fishes. *Transgenic Res* 2017; 26(5): 577-89.  
[http://dx.doi.org/10.1007/s11248-017-0030-5] [PMID: 28681201]
- [55] Tao B, Tan J, Chen L, et al. CRISPR/Cas9 system-based myostatin-targeted disruption promotes somatic growth and adipogenesis in loach, *Misgurnus anguillicaudatus*. *Aquaculture* 2021; 544: 737097.  
[http://dx.doi.org/10.1016/j.aquaculture.2021.737097]
- [56] Xu C, Wu G, Zohar Y, Du SJ. Analysis of *myostatin* gene structure, expression and function in zebrafish. *J Exp Biol* 2003; 206(22): 4067-79.  
[http://dx.doi.org/10.1242/jeb.00635] [PMID: 14555747]
- [57] Aiello D, Patel K, Lasagna E. The *myostatin* gene: an overview of mechanisms of action and its relevance to livestock animals. *Anim Genet* 2018; 49(6): 505-19.  
[http://dx.doi.org/10.1111/age.12696] [PMID: 30125951]
- [58] Miramontes E, Kempisty B, Petite J, et al. Myogenic response to increasing concentrations of ammonia differs between mammalian, avian, and fish species: cell differentiation and genetic study. *Genes (Basel)* 2020; 11(8): 840.  
[http://dx.doi.org/10.3390/genes11080840] [PMID: 32722004]
- [59] Radaelli G, Rowlerson A, Mascarello F, Patruno M, Funkenstein B. Myostatin precursor is present in several tissues in teleost fish: a comparative immunolocalization study. *Cell Tissue Res* 2003; 311(2): 239-50.  
[http://dx.doi.org/10.1007/s00441-002-0668-y] [PMID: 12596043]
- [60] Wang C, Chen YL, Bian WP, et al. Deletion of *mstna* and *mstnb* impairs the immune system and affects growth performance in zebrafish. *Fish Shellfish Immunol* 2018; 72: 572-80.  
[http://dx.doi.org/10.1016/j.fsi.2017.11.040] [PMID: 29175471]
- [61] Ge L, Dong X, Gong X, Kang J, Zhang Y, Quan F. Mutation in myostatin 3'UTR promotes C2C12 myoblast proliferation and differentiation by blocking the translation of MSTN. *Int J Biol Macromol* 2020; 154: 634-43.  
[http://dx.doi.org/10.1016/j.ijbiomac.2020.03.043] [PMID: 32156541]
- [62] Zhang S, Li Y, Shao J, et al. Functional identification and characterization of IpMSTNa, a novel orthologous myostatin (MSTN) gene in channel catfish *Ictalurus punctatus*. *Int J Biol Macromol* 2020; 152: 1-10.  
[http://dx.doi.org/10.1016/j.ijbiomac.2020.02.060] [PMID: 32045608]
- [63] Berg RT, Shahin A. Double muscling: More and better beef. In: *Beef Cattle Science Handbook*. CRC Press 2019; pp. 560-70.
- [64] Deng B, Zhang F, Wen J, et al. The function of myostatin in the regulation of fat mass in mammals. *Nutr Metab (Lond)* 2017; 14(1): 29.  
[http://dx.doi.org/10.1186/s12986-017-0179-1] [PMID: 28344633]
- [65] Rebhan Y, Funkenstein B. Inhibition of fish myostatin activity by recombinant fish follistatin and myostatin prodomain: Potential implications for enhancing muscle growth in farmed fish. *Aquaculture* 2008; 284(1-4): 231-8.  
[http://dx.doi.org/10.1016/j.aquaculture.2008.07.007]
- [66] Gao Y, Dai Z, Shi C, et al. Depletion of myostatin b promotes somatic growth and lipid metabolism in zebrafish. *Front Endocrinol (Lausanne)* 2016; 7: 88.  
[http://dx.doi.org/10.3389/fendo.2016.00088] [PMID: 27458428]
- [67] Vianello S, Brazzoduro L, Dalla Valle L, Belvedere P, Colombo L. Myostatin expression during development and chronic stress in zebrafish (*Danio rerio*). *J Endocrinol* 2003; 176(1): 47-59.  
[http://dx.doi.org/10.1677/joe.0.1760047] [PMID: 12525249]
- [68] Zhong Z, Niu P, Wang M, et al. Targeted disruption of *sp7* and myostatin with CRISPR-Cas9 results in severe bone defects and more muscular cells in common carp. *Sci Rep* 2016; 6(1): 22953.  
[http://dx.doi.org/10.1038/srep22953] [PMID: 26976234]
- [69] Khalil K, Elayat M, Khalifa E, et al. Generation of myostatin gene-edited channel catfish (*Ictalurus punctatus*) via zygote injection of CRISPR/Cas9 system. *Sci Rep* 2017; 7(1): 7301.  
[http://dx.doi.org/10.1038/s41598-017-07223-7] [PMID: 28779173]
- [70] Sun Y, Zheng GD, Nissa M, Chen J, Zou SM. Disruption of *mstna* and *mstnb* gene through CRISPR/Cas9 leads to elevated muscle mass in blunt snout bream (*Megalobrama amblycephala*). *Aquaculture* 2020; 528: 735597.  
[http://dx.doi.org/10.1016/j.aquaculture.2020.735597]
- [71] Feldman BJ, Streeper RS, Farese RV Jr, Yamamoto KR. Myostatin modulates adipogenesis to generate adipocytes with favorable metabolic effects. *Proc Natl Acad Sci USA* 2006; 103(42): 15675-80.  
[http://dx.doi.org/10.1073/pnas.0607501103] [PMID: 17030820]
- [72] Xin XB, Yang SP, Li X, et al. Proteomics insights into the effects of MSTN on muscle glucose and lipid metabolism in genetically edited cattle. *Gen Comp Endocrinol* 2020; 291: 113237.  
[http://dx.doi.org/10.1016/j.ygcen.2019.113237] [PMID: 31374285]
- [73] Guo T, Jou W, Chanturiya T, Portas J, Gavrilova O, McPherron AC. Myostatin inhibition in muscle, but not adipose tissue, decreases fat mass and improves insulin sensitivity. *PLoS One* 2009; 4(3): e4937.  
[http://dx.doi.org/10.1371/journal.pone.0004937] [PMID: 19295913]
- [74] Artaza JN, Bhasin S, Magee TR, et al. Myostatin inhibits myogenesis and promotes adipogenesis in C3H 10T1/2 mesenchymal multipotent cells. *Endocrinology* 2005; 146(8): 3547-57.  
[http://dx.doi.org/10.1210/en.2005-0362] [PMID: 15878958]
- [75] Zhao B, Wall RJ, Yang J. Transgenic expression of myostatin propeptide prevents diet-induced obesity and insulin resistance. *Biochem Biophys Res Commun* 2005; 337(1): 248-55.  
[http://dx.doi.org/10.1016/j.bbrc.2005.09.044] [PMID: 16182246]
- [76] Mosler S, Relizani K, Mouisel E, Amthor H, Diel P. Combinatory effects of siRNA-induced myostatin inhibition and exercise on skeletal muscle homeostasis and body composition. *Physiol Rep* 2014; 2(3): e00262.  
[http://dx.doi.org/10.1002/phy2.262] [PMID: 24760516]
- [77] McPherron AC, Guo T, Wang Q, Portas J. Soluble activin receptor type IIB treatment does not cause fat loss in mice with diet-induced obesity. *Diabetes Obes Metab* 2012; 14(3): 279-82.  
[http://dx.doi.org/10.1111/j.1463-1326.2011.01520.x] [PMID: 22023380]
- [78] Dong J, Dong Y, Dong Y, Chen F, Mitch WE, Zhang L. Inhibition of myostatin in mice improves insulin sensitivity via irisin-mediated cross talk between muscle and adipose tissues. *Int J Obes* 2016; 40(3): 434-42.  
[http://dx.doi.org/10.1038/ijo.2015.200] [PMID: 26435323]
- [79] Galt NJ, Froehlich JM, Meyer BM, Barrows FT, Biga PR. High-fat diet reduces local myostatin-1 paralog expression and alters skeletal muscle lipid content in rainbow trout, *Oncorhynchus mykiss*. *Fish Physiol Biochem* 2014; 40(3): 875-86.  
[http://dx.doi.org/10.1007/s10695-013-9893-4] [PMID: 24264425]
- [80] Kishimoto K, Washio Y, Yoshiura Y, et al. Production of a breed of red sea bream *Pagrus major* with an increase of skeletal muscle mass and reduced body length by genome editing with CRISPR/Cas9. *Aquaculture* 2018; 495: 415-27.  
[http://dx.doi.org/10.1016/j.aquaculture.2018.05.055]
- [81] Ohama M, Washio Y, Kishimoto K, Kinoshita M, Kato K. Growth performance of myostatin knockout red sea bream *Pagrus major* juveniles produced by genome editing with CRISPR/Cas9. *Aquaculture* 2020; 529: 735672.  
[http://dx.doi.org/10.1016/j.aquaculture.2020.735672]
- [82] The role of the myostatin protein in meat quality—a review. *Arch Tierzucht* 2002; 45(2): 159-70.
- [83] Chen PR, Lee K. INVITED REVIEW: Inhibitors of myostatin as methods of enhancing muscle growth and development1. *J Anim Sci* 2016; 94(8): 3125-34.  
[http://dx.doi.org/10.2527/jas.2016-0532] [PMID: 27695802]

[84] Lach-Trifilieff E, Minetti GC, Sheppard K, *et al.* An antibody blocking activin type II receptors induces strong skeletal muscle hypertrophy and protects from atrophy. *Mol Cell Biol* 2014; 34(4): 606-18. [<http://dx.doi.org/10.1128/MCB.01307-13>] [PMID: 24298022]

[85] Omairi S, Matsakas A, Degens H, *et al.* Enhanced exercise and regenerative capacity in a mouse model that violates size constraints of oxidative muscle fibres. *eLife* 2016; 5: e16940. [<http://dx.doi.org/10.7554/eLife.16940>] [PMID: 27494364]

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