© 2023 Google LLC Liver King is natty? He confesses to have done Gene Editing in Singapore in 2018. Check out this video for more details.

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The potential for gene-editing to increase muscle growth in pigs .

Dilger et al. CABI Agriculture and Bioscience (2022) 3:36
https://doi.org/10.1186/s43170-022-00106-6

CABI Agriculture and Bioscience

REVIEW Open Access

The potential for gene-editing to increase muscle growth in pigs: experiences with editing myostatin

A. C. Dilger[1*], X. Chen[1], L. T. Honegger[1], B. M. Marron[1] and J. E. Beever[2]

Abstract

Gene-editing holds promise as a new technique for growth promotion in livestock, especially in the face of increased opposition to traditional methods of growth promotion like feed additives. However, to date, there has been only limited progress toward models of growth promotion through gene-editing. The vast majority of gene-editing projects have focused on a single gene, myostatin (*MSTN*), with several reports of successful editing events. These attempts have been limited by the low efficiency of successful edits and issues of viability. The use of both microinjection and somatic cell nuclear transfer appear to be susceptible to these viability issues. Herein, we report a successful editing of myostatin in pigs using a zinc-finger nuclease targeted at exon 3 of myostatin. Overall, the successful editing rate was 1% (37 edited cell lines/3616 screened cell lines). Edits included a variety of small indels and larger deletions. One male and one female cell line with a deletion of one thymidine residue (− 1 T) were selected for somatic cell nuclear transfer. Of the ~ 900 embryos transferred, there were 12 live births (1 male, 11 females) but only 5 female pigs survived to sexual maturity. These animals were bred to commercial sires to expand the population and determine potential interactive effects between myostatin mutations and the naturally-occurring g.3072G > A mutation in insulin-like growth factor 2. Even in subsequent generations (F0xWT, F1xF0, F1xF1), viability of piglets continued to be poor and was associated with the progeny's proportion of the original clone genome, even in pigs lacking *MSTN* loss-of-function (LOF) mutations. However, viability of pigs with myostatin LOF ($MSTN^{-/-}$) was especially poor as none of the 37 animals born were viable. Sequencing of cloned pigs indicated that off-target effects did not explain this poor viability. Reducing the percentage of the cloned genome by outcrossing successfully improved viability of $MSTN^{+/+}$ and $MSTN^{\Delta}$ pigs, but not of $MSTN^{-/-}$ pigs. Characterization of $MSTN^{\Delta}$ pigs did reveal an increase in muscle growth and body weight compared with $MSTN^{+/+}$ pigs. Therefore, in order for the promise of gene-editing of myostatin for growth promotion in livestock to be fulfilled, issues of viability of offspring and efficacy of editing have yet to be overcome. Additionally, gene-editing targets other than myostatin must be explored.

Keywords: Gene-editing, Growth, Livestock, Myostatin, Muscle, Pig, Zinc-finger nuclease

Background

In the next 30 years, the world population is predicted to increase to between 9.5 and 10 billion people, resulting in an increased demand for food. In particular, the demand for animal-derived protein is expected to increase 50–100%. While alternative proteins like those from plant-based meat substitutes or derived from cultured cells may help in meeting this demand, a large part

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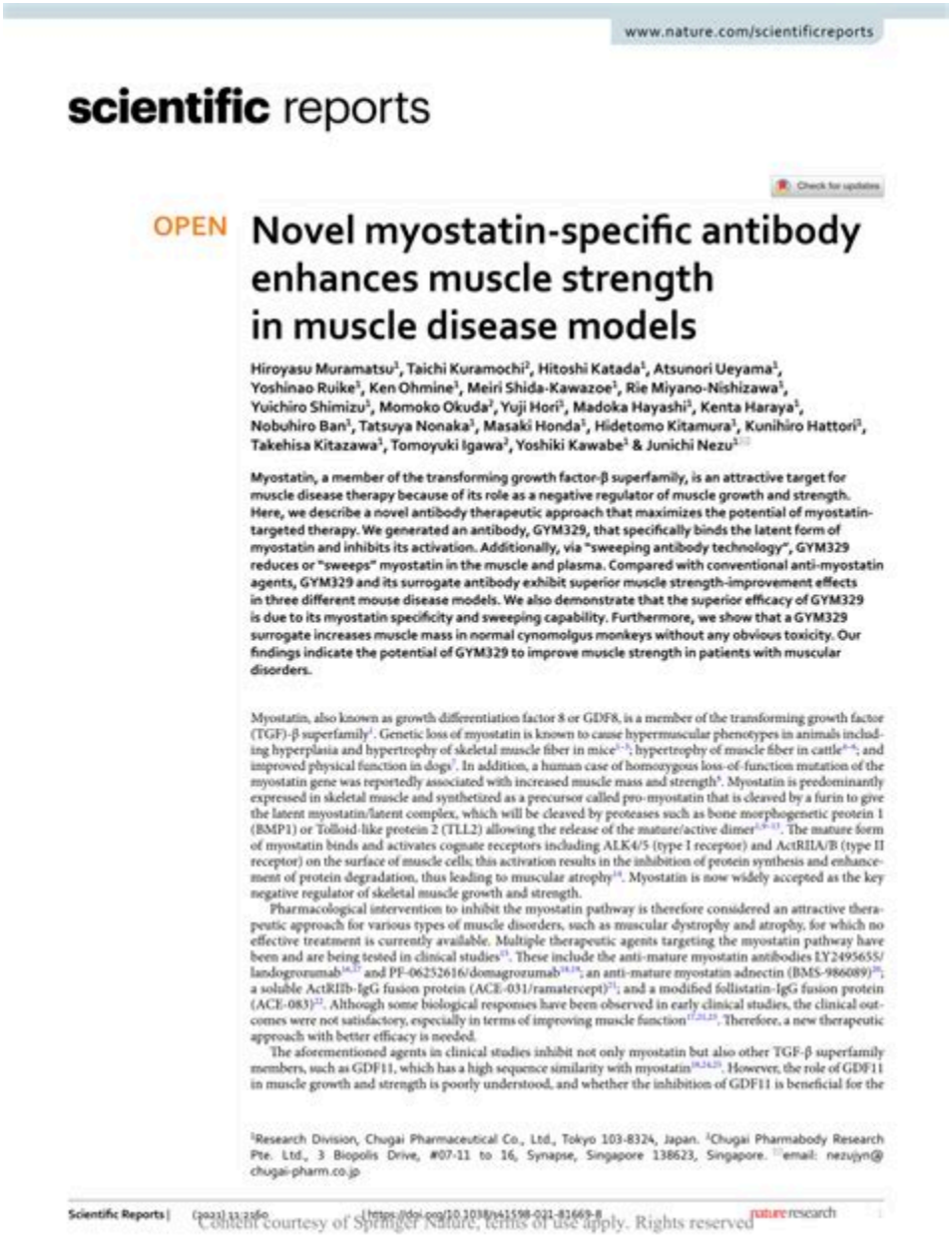
Full list of author information is available at the end of the article

And the liver king is most def not natty . that absolute cutting edge of crispr to gene edit out myostatin. This actually made me read a few medical articles out of curiosity. Unfortunately this isn't something any doctor would perform. . Damn Gimley got jacked…that gene editing is the shit

Novel myostatin-specific antibody enhances muscle strength in . - Nature



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Novel myostatin-specific antibody enhances muscle strength in muscle disease models

Hiroyasu Muramatsu[1], Taichi Kuramochi[2], Hitoshi Katada[1], Atsunori Ueyama[1], Yoshinao Ruike[1], Ken Ohmine[1], Meiri Shida-Kawazoe[1], Rie Miyano-Nishizawa[1], Yuichiro Shimizu[1], Momoko Okuda[2], Yuji Hori[2], Madoka Hayashi[2], Kenta Haraya[1], Nobuhiro Ban[1], Tatsuya Nonaka[1], Masaki Honda[1], Hidetomo Kitamura[1], Kunihiro Hattori[1], Takehisa Kitazawa[1], Tomoyuki Igawa[2], Yoshiki Kawabe[1] & Junichi Nezu[1]

Myostatin, a member of the transforming growth factor-β superfamily, is an attractive target for muscle disease therapy because of its role as a negative regulator of muscle growth and strength. Here, we describe a novel antibody therapeutic approach that maximizes the potential of myostatin-targeted therapy. We generated an antibody, GYM329, that specifically binds the latent form of myostatin and inhibits its activation. Additionally, via "sweeping antibody technology", GYM329 reduces or "sweeps" myostatin in the muscle and plasma. Compared with conventional anti-myostatin agents, GYM329 and its surrogate antibody exhibit superior muscle strength-improvement effects in three different mouse disease models. We also demonstrate that the superior efficacy of GYM329 is due to its myostatin specificity and sweeping capability. Furthermore, we show that a GYM329 surrogate increases muscle mass in normal cynomolgus monkeys without any obvious toxicity. Our findings indicate the potential of GYM329 to improve muscle strength in patients with muscular disorders.

Myostatin, also known as growth differentiation factor 8 or GDF8, is a member of the transforming growth factor (TGF)-β superfamily[1]. Genetic loss of myostatin is known to cause hypermuscular phenotypes in animals including hyperplasia and hypertrophy of skeletal muscle fiber in mice[2–5]; hypertrophy of muscle fiber in cattle[6–8]; and improved physical function in dogs[9]. In addition, a human case of homozygous loss-of-function mutation of the myostatin gene was reportedly associated with increased muscle mass and strength[3]. Myostatin is predominantly expressed in skeletal muscle and synthetized as a precursor called pro-myostatin that is cleaved by a furin to give the latent myostatin/latent complex, which will be cleaved by proteases such as bone morphogenetic protein 1 (BMP1) or Tolloid-like protein 2 (TLL2) allowing the release of the mature/active dimer[4,9–13]. The mature form of myostatin binds and activates cognate receptors including ALK4/5 (type I receptor) and ActRIIA/B (type II receptor) on the surface of muscle cells; this activation results in the inhibition of protein synthesis and enhancement of protein degradation, thus leading to muscular atrophy[14]. Myostatin is now widely accepted as the key negative regulator of skeletal muscle growth and strength.

Pharmacological intervention to inhibit the myostatin pathway is therefore considered an attractive therapeutic approach for various types of muscle disorders, such as muscular dystrophy and atrophy, for which no effective treatment is currently available. Multiple therapeutic agents targeting the myostatin pathway have been and are being tested in clinical studies[15]. These include the anti-mature myostatin antibodies LY2495655/landogrozumab[16,17] and PF-06252616/domagrozumab[18,19]; an anti-mature myostatin adnectin (BMS-986089)[20]; a soluble ActRIIb-IgG fusion protein (ACE-031/ramatercept)[21]; and a modified follistatin-IgG fusion protein (ACE-083)[22]. Although some biological responses have been observed in early clinical studies, the clinical outcomes were not satisfactory, especially in terms of improving muscle function[17,21,23]. Therefore, a new therapeutic approach with better efficacy is needed.

The aforementioned agents in clinical studies inhibit not only myostatin but also other TGF-β superfamily members, such as GDF11, which has a high sequence similarity with myostatin[18,24,25]. However, the role of GDF11 in muscle growth and strength is poorly understood, and whether the inhibition of GDF11 is beneficial for the

[1]Research Division, Chugai Pharmaceutical Co., Ltd., Tokyo 103-8324, Japan. [2]Chugai Pharmabody Research Pte. Ltd., 3 Biopolis Drive, #07-11 to 16, Synapse, Singapore 138623, Singapore. ✉email: nezujyn@chugai-pharm.co.jp

0:00 / 7:45 Liver King CLAIMS he had MYOSTATIN GENE EDITING Done in Singapore | @KENNYKO 's Natty Or Not Ryan Russo 52K subscribers Subscribe 358 11K views 4 months ago #LiverKing #Primal.

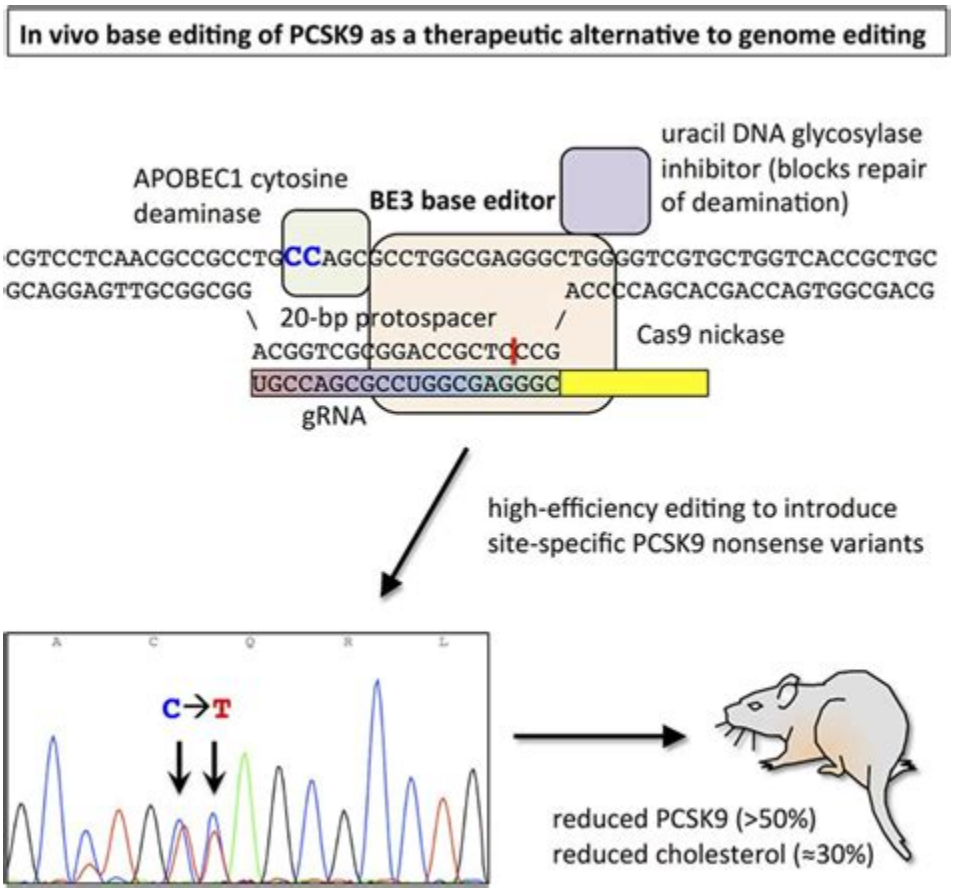
Liver King is jacked from a new procedure: Myostatin Gene Editing .

Bodybuilding Video: Kenny KO Confronts Liver King Face to Face on Natty or Not Status and Ab Implants Kenny KO didn't hold back in asking Liver King some pressing questions about steroids and whether or not he's had ab surgery/implants. Written by Doug Murray Last Updated on September 19, 2022 Kenny KO & Liver King (Credit: @kenykoooo/Instagram)

Myostatin is associated with the presence and development of acute-on .

Liver King Had Myostatin Gene Editing! Not Steroids! Aaron Olson 2. 27K subscribers 7. 4K views 9 months ago Liver King tells how he was the first human to have myostatin gene.

Therapeutic base editing in the adult liver | Nature Reviews .

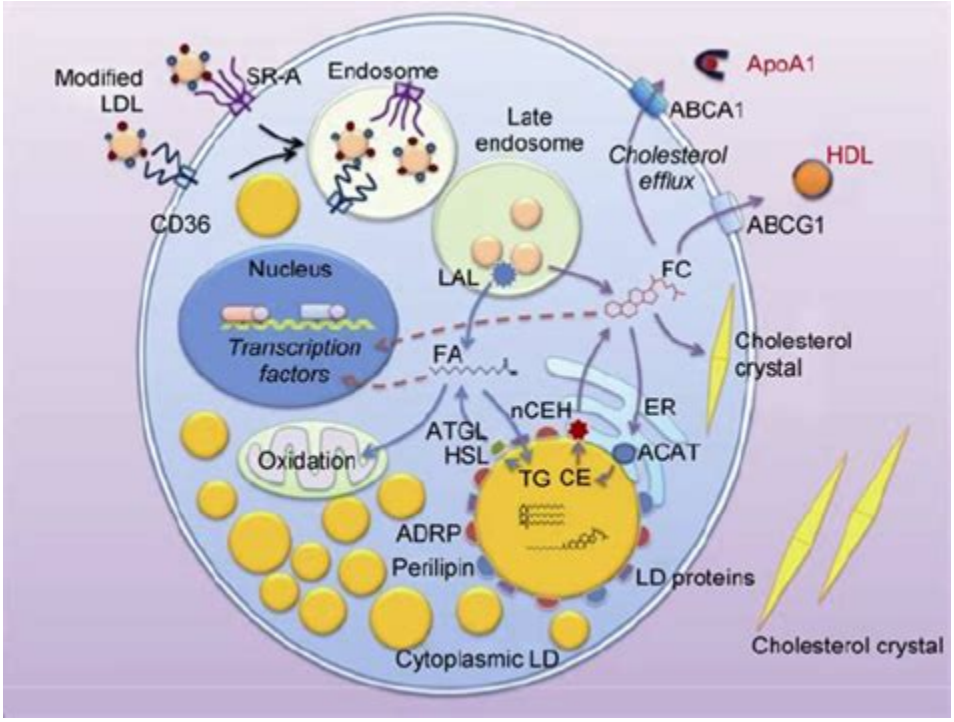


The vast majority of gene-editing projects have focused on a single gene, myostatin (MSTN), with several reports of successful editing events. These attempts have been limited by the low efficiency of successful edits and issues of viability.

Liver King Confesses To Gene Editing For His Muscles - YouTube

Background Elevated plasma levels of the branched-chain amino acid (BCAA) leucine are associated with obesity and insulin resistance (IR), and thus the propensity for type 2 diabetes mellitus development. However, other clinical studies suggest the contradictory view that leucine may in fact offer a degree of protection against metabolic syndrome. Aiming to resolve this apparent paradox, we .

Leucine alters hepatic glucose/lipid homeostasis via the myostatin-AMP .



Introduction. Myostatin (MSTN) is a transforming growth factor-β family member that plays a critical role in negatively regulating skeletal muscle mass. 1 Genetic studies have demonstrated that myostatin gene deficiency leads to muscle hypertrophy due to a combination of increased fiber numbers and increased fiber sizes in multiple species including human, 2 cattle, 3, 4, 5 mouse, 1 sheep, 6 .

Video: Kenny KO Confronts Liver King Face to Face on Natty or Not .

1 2 3 4 5 6 7 PMID: 37554924 PMCID: PMC10405090 DOI: 10. 1016/j. jhepr. 2023. 100761
Background & aims: Acute-on-chronic liver failure (ACLF) has been linked to different pathophysiological mechanisms, including systemic inflammation and mitochondrial dysfunction.

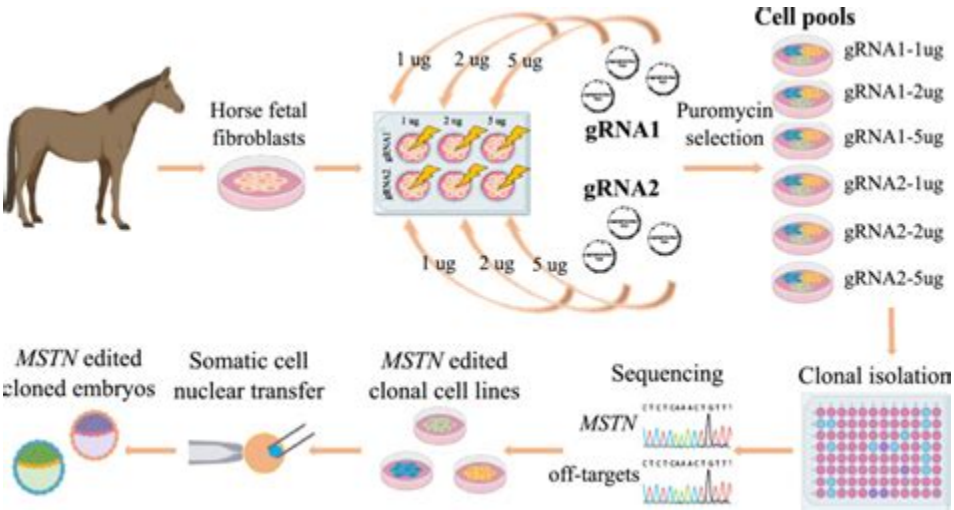
Soooooo, not natty then : r/facepalm - Reddit

Myostatin is a muscle hormone, it is decreased in patients with muscle loss and is a marker of impaired muscle function. In this study we show that myostatin levels are decreased in patients with cirrhosis, with lower levels in patients with acute decompensation and acute-on chronic liver failure (ACLF).

Liver King CLAIMS he had MYOSTATIN GENE EDITING Done in . - YouTube

This is the first report describing the effects of long-term, systemic myostatin inhibition in a large-animal model of DMD, and we believe that the simple and effective nature of our liver-directed gene-transfer strategy makes it an ideal candidate for evaluation as a novel therapeutic approach for DMD patients. Go to: Introduction

Generation of myostatin edited horse embryos using CRISPR/Cas9 . - Nature



We found that both rAAV-SaCas9 systems had gene editing efficiency, reducing the expression of myostatin by affecting the relevant signaling pathways, thereby altering the physiological status.

Antimyostatin Treatment in Health and Disease: The Story of Great .

cells

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Review

Antimyostatin Treatment in Health and Disease: The Story of Great Expectations and Limited Success

Tue L. Nielsen *, John Vissing and Thomas O. Krag

Copenhagen Neuromuscular Center, Department of Neurology, Rigshospitalet, University of Copenhagen, DK-2100 Copenhagen, Denmark; john.vissing@regionh.dk (J.V.); thomas.krag@regionh.dk (T.O.K.)
* Correspondence: tue.leth.nielsen.01@regionh.dk

Abstract: In the past 20 years, myostatin, a negative regulator of muscle mass, has attracted attention as a potential therapeutic target in muscular dystrophies and other conditions. Preclinical studies have shown potential for increasing muscular mass and ameliorating the pathological features of dystrophic muscle by the inhibition of myostatin in various ways. However, hardly any clinical trials have proven to translate the promising results from the animal models into patient populations. We present the background for myostatin regulation, clinical and preclinical results and discuss why translation from animal models to patients is difficult. Based on this, we put the clinical relevance of future antimyostatin treatment into perspective.

Keywords: myostatin; muscular dystrophy; muscular regeneration; ActRIIB; TGF-β

Citation: Nielsen, T.L.; Vissing, J.; Krag, T.O. Antimyostatin Treatment in Health and Disease: The Story of Great Expectations and Limited Success. *Cells* **2021**, *10*, 533. https://doi.org/10.3390/cells10030533

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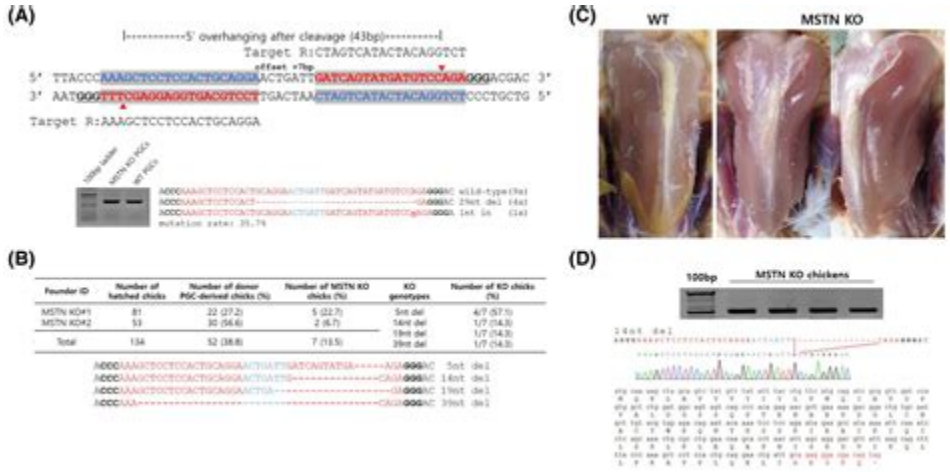
1. Introduction

Muscular dystrophies consist of a broad array of inherited conditions characterized by muscular wasting and atrophy. As clinical presentations in patients may vary due to a wide spectrum of phenotype–genotype variants for a particular gene, a common treatment, not depending on correcting a single molecular defect, has emerged as an attractive target for development. For the last 20 years, one of the most promising therapeutic subjects in the field of muscular dystrophies has been myostatin. Identified for the first time in 1997, myostatin knock-out in mice caused increased muscle mass [1] and mutations in the myostatin gene (*MSTN*) gene have subsequently been identified in the double muscled Belgian Blue and Piedmontese cattle [2–4] as well as whippet racing dogs [5]. In 2004, a loss-of-function mutation of *MSTN* in a German boy with a hypermuscular phenotype demonstrated that the effect of myostatin is functionally conserved across different mammalian species [6]. Since myostatin loss of function did not appear to have any negative impact on viability and longevity [7,8], interest was raised towards a novel treatment by harnessing the potential of inhibiting this negative regulator of muscular growth. Numerous studies in animal models and clinical trials have tried to explore this relationship with promising results in preclinical studies, which have translated poorly in human clinical studies. As the molecular and preclinical foundation for myostatin inhibition have been carefully reviewed before [9,10], this review will briefly describe the molecular involvement of myostatin in the muscle of humans and mice as well as healthy, diseased and exercising individuals. We will focus on the detailed results of the preclinical studies, the common denominators of these and we will present the results of the clinical trials in humans and how results in mice may or may not translate to humans. Finally, we offer perspective to a future path for myostatin inhibition with respect to the knowledge that the past 20 years of myostatin research has provided us with.

Background While product of the myostatin gene (MSTN) is an important factor influencing muscle growth, which is well confirmed in nonhuman species, it has not been clearly confirmed whether MSTN expression influences interindividual differences in skeletal muscle mass, affects posttraining changes, or plays a role in the age-related loss of muscle mass and function in humans. Although the .

Generation of myostatin-knockout chickens mediated by D10A-Cas9 nickase .



Liver King is jacked from a new procedure: Myostatin Gene Editing. What the fuk? This is a thing you can do? The secret behind building healthy insane muscle mass: just edit your fukin myostatin gene 09-22-2022, 06:39 AM #2 Duckliver Offal Join Date: Jun 2013 Location: Washington, United States Posts: 17,751 Rep Power: 286835

Liver King Had Myostatin Gene Editing! Not Steroids! - YouTube

This technology incorporates two core elements into the "sweeping antibody": (1) a fragment crystallizable (Fc) domain with enhanced affinity to the FcγRIIb receptor, and (2) an antigen-binding.

Improvement of muscular atrophy by AAV-SaCas9-mediated myostatin gene .

Cancer Gene Therapy
https://doi.org/10.1038/s41417-020-0178-7

ARTICLE

Improvement of muscular atrophy by AAV–SaCas9-mediated myostatin gene editing in aged mice

Shaoting Weng[1] · Feng Gao[1] · Juan Wang[1] · Xingyu Li[1] · Beibei Chu[1] · Jiang Wang[1] · Guoyu Yang[1]

Received: 13 February 2020 / Revised: 9 April 2020 / Accepted: 24 April 2020

Abstract
Muscle mass and area usually decrease with age, and this phenomenon is known as sarcopenia. This age-related atrophy correlates with insufficient levels of muscle cells differentiate and proliferate regulated by the TGF-β signaling pathway and the expression of E3s ubiquitin-protein ligase by the aged. Sarcopenia makes a huge impact on the aging society, because it has the characteristic of high incidence, extensive adverse effects and disease aggravation gradually. Guided by a single-guide RNA (sgRNA), Cas9 nuclease has been widely used in genome editing, opening up a new pathway for sarcopenia treatment. Here, we present two rAAV9 systems, pX601-AAV-CMV:SaCas9-U6:sgRNA and pX601-AAV-EF1α:SaCas9-$tRNA_{GLN}$: sgRNA, which edited myostatin efficiently. By delivering the two rAAV–SaCas9 targets to myostatin via intramuscular injection of aged mice, an increase in body weight and an increase in the number and area of myofibers were observed. Knockout of myostatin led to TGF-β signaling pathway changes, and increased MyoD, Pax7 and MyoG protein levels and increased the number of satellite cells to improve muscle cells differentiation. Moreover, knockout of myostatin prevented the atrophy of muscle cells through reduced Murf1 and MAFbx protein levels. We found that both rAAV–SaCas9 systems had gene editing efficiency, reducing the expression of myostatin by affecting the relevant signaling pathways, thereby altering the physiological status. We showed that myostatin has an important role in activating skeletal muscle proliferation and inhibiting muscular atrophy during aging. Thus, we propose that knockout of myostatin using the rAAV9–SaCas9 system has significant therapeutic potential in sarcopenia.

Introduction

Cas9 is an RNA-guided endonuclease derived from the type II CRISPR–Cas adaptive immune system of bacterial adaptive immune system. Because of its small size, strong targeting and high editing efficiency, it has been widely used in genome editing and has a broad application prospect in disease therapy. However, genome editing of tissue in post-natal animals is restricted because of the challenge of delivering Cas9 in vivo. In recent years, recombinant adeno-associated virus (rAAV) as a promising gene delivery vector, has been widely used in genome editing at the animal level. The application of this vector in gene therapy possesses several advantages, including extensive serotype specificity, a low oncogenic risk of host-genome integration and low immunogenicity. However, the restrictive cargo size (~4.5 kb) of AAV limit the ability to packaging the commonly used *Streptococcus pyogenes* Cas9 (SpCas9, ~4.2 kb) and its single-guide RNA (sgRNA) into a single vector. The compact SaCas9 (~3.3 kb) which is derived from *Staphylococcus aureus*, is smaller and possesses a more specific protospacer adjacent motif (PAM) than SpCas9, which makes it suitable for delivery using AAV vector. Ran et al. [1] reported that SaCas9 can edit the genome with efficiencies similar to those of SpCas9, and packaged SaCas9 and its sgRNA into a single AAV vector, thus significantly reducing expression level of cholesterol by knocked out Pcsk9 in the mouse liver. El Refaey et al. [2] showed that a single systemic AAV–SaCas9 could

Supplementary information The online version of this article (https://doi.org/10.1038/s41417-020-0178-7) contains supplementary material, which is available to authorized users.

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Published online: 13 May 2020

Identified for the first time in 1997, myostatin knock-out in mice caused increased muscle mass [1] and mutations in the myostatin gene (MSTN) gene have subsequently been identified in the double muscled Belgian Blue and Piedmontese cattle [2, 3, 4] as well as whippet racing dogs [5].

Targeted Myostatin Gene Editing in Multiple Mammalian Species Directed .

Citation: Molecular Therapy—Nucleic Acids (2013) 2, e112; doi:10.1038/mtna.2013.39

www.nature.com/mtna

Targeted Myostatin Gene Editing in Multiple Mammalian Species Directed by a Single Pair of TALE Nucleases

Li Xu[1], Piming Zhao[1], Andrew Mariano[1] and Renzhi Han[1]

Myostatin (MSTN) is a negative regulator of skeletal muscle mass. Strategies to block myostatin signaling pathway have been extensively pursued to increase muscle mass in various disease settings including muscular dystrophy. Here, we report a new class of reagents based on transcription activator-like effector nucleases (TALENs) to disrupt myostatin expression at the genome level. We designed a pair of MSTN TALENs to target a highly conserved sequence in the coding region of the myostatin gene. We demonstrate that codelivery of these MSTN TALENs induce highly specific and efficient gene disruption in a variety of human, cattle, and mouse cells. Based upon sequence analysis, this pair of TALENs is expected to be functional in many other mammalian species. Moreover, we demonstrate that these MSTN TALENs can facilitate targeted integration of a mCherry expression cassette or a larger muscular dystrophy gene (dysferlin) expression cassette into the *MSTN* locus in mouse or human cells. Therefore, targeted editing of the myostatin gene using our highly specific and efficient TALEN pair would facilitate cell engineering, allowing potential use in translational research for cell-based therapy.

Molecular Therapy—Nucleic Acids (2013) **2**, e112; doi:10.1038/mtna.2013.39; published online 30 July 2013
Subject Category: Gene insertion, deletion & modification

Introduction

Myostatin (MSTN) is a transforming growth factor-β family member that plays a critical role in negatively regulating skeletal muscle mass.[1] Genetic studies have demonstrated that myostatin gene deficiency leads to muscle hypertrophy due to a combination of increased fiber numbers and increased fiber sizes in multiple species including human,[2] cattle,[3–5] mouse,[1] sheep,[6] and dog[7] without causing severe adverse consequences. Therefore, extensive efforts have been undertaken to develop effective strategies for blocking the myostatin signaling pathway as therapies for various muscle-wasting diseases such as muscular dystrophy, sarcopenia, and long bedding patients.[8–12] Indeed, myostatin inhibitors have shown great promise to significantly increase muscle growth in model animals.[8,13–15]

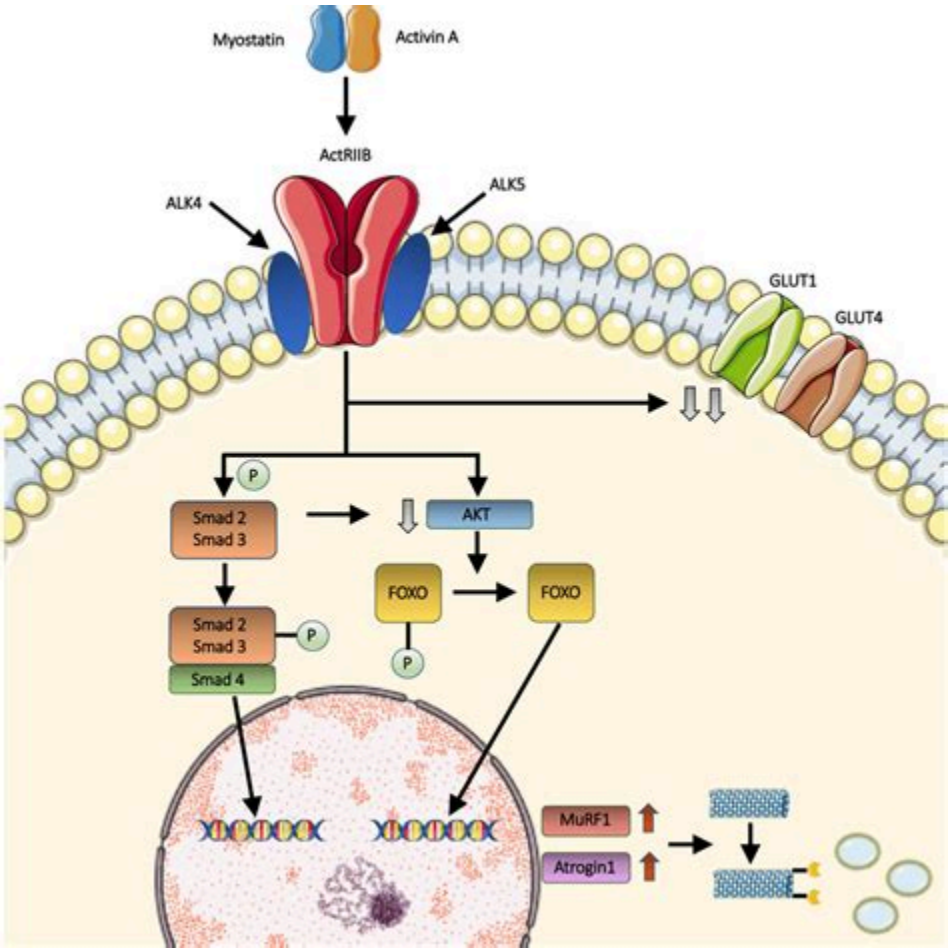
Targeting the *MSTN* gene would provide a permanent solution to block myostatin signaling. However, conventional gene targeting approach has been limited to mouse embryonic stem cells and not readily adaptable for most other cell types because of the extremely low targeting frequency. Recent studies have shown that targeted genome editing with minimal toxicity in many different types of cells is possible by combining engineered zinc finger nucleases (ZFNs) with inherent DNA repair mechanisms within the cell.[17] It has been shown that ZFNs promote genome editing via nonhomologous end-joining (NHEJ) and homology-directed DNA repair by creating a double-strand break at a specific target locus.[18] A typical nuclease is composed of two essential domains: the DNA-binding domain and the nonspecific cleavage domain of the FokI restriction enzyme. The DNA-binding domain, which is composed of multiple zinc finger arrays, can be re-engineered to bind to a wide variety of DNA sequences, making it possible to engineer ZFNs which specifically target the user-defined sequences. ZFN-facilitated genome editing allows stable integration of therapeutic genes or restoration of mutated genes in specific genetic loci.[19] It thus offers a promising approach for treating genetic disorders and has gained much research interest recently. Since the first seminal publications about ZFNs in the late 1990s,[18,20,21] many ZFNs have been successfully engineered to perform genome editing in cells of several different species, including human and mouse. ZFN-mediated *in vivo* genome editing was recently shown to restore hemostasis in a mouse model of hemophilia via adeno-associated virus-mediated delivery of ZFNs and a donor gene into the mouse liver,[22] and ZFN-mediated CCR5 gene knockout is currently in clinical trial for establishing HIV-1 resistance in CD4$^+$ T cells.[23] These exciting progresses raise the possibility of genome editing as a viable strategy to treat diseases caused by genetic mutation. However, there is still a lack of an optimal strategy to engineering highly active and specific ZFNs.

Recently, a new class of nucleases called transcription activator-like effector nucleases (TALENs), which contain DNA-binding domains based on transcription activator-like effector (TALE) proteins from *Xanthomonas* plant pathogens, have emerged.[24–27] The central repeat domain in the TALE structure mediates DNA binding with each repeat specifying one target base. The base preference of each repeat is determined by two critical, adjacent amino acids referred to as the "repeat variable di-residue" (RVD) which preferentially recognizes one of the four bases in the target site.[28,29] This simple "two amino acids for one base" code enables rapid engineering of customized TALE repeat arrays that recognize a user-defined target sequence. It has been shown that unique TALE-binding sites can be found on average every 35 base pairs,[27] making it highly attractive for scientific laboratories to practice gene editing in various cell types.

[1]Department of Cell and Molecular Physiology, Loyola University Chicago Health Science Division, Maywood, Illinois. Correspondence: Renzhi Han, Department of Cell and Molecular Physiology, Loyola University Chicago Health Science Division, Maywood, Illinois. E-mail: renhan@lumc.edu
Keywords: dysferlin; gene editing; myostatin; TALEN
Received 18 January 2013; accepted 12 June 2013; advance online publication 30 July 2013. doi:10.1038/mtna.2013.39

Ren, Xiao et al. identify a mechanism by which myostatin regulates adipogenesis, using myostatin-knockout pigs. Myostatin deficiency upregulates MEF2C that binds to the promoter of miR222. miR222 .

Genetic variants in myostatin and its receptors promote elite athlete .



Myostatin (MSTN), a member of the transforming growth factor-β superfamily, is a negative regulator of muscle growth and development. Disruption of the MSTN gene in various mammalian species markedly promotes muscle growth. Previous studies have mainly focused on the disruption of the MSTN peptide c …

Myostatin regulates fatty acid desaturation and fat deposition through .

COMMUNICATIONS BIOLOGY

ARTICLE

https://doi.org/10.1038/s42003-020-01348-8 OPEN

Myostatin regulates fatty acid desaturation and fat deposition through MEF2C/miR222/SCD5 cascade in pigs

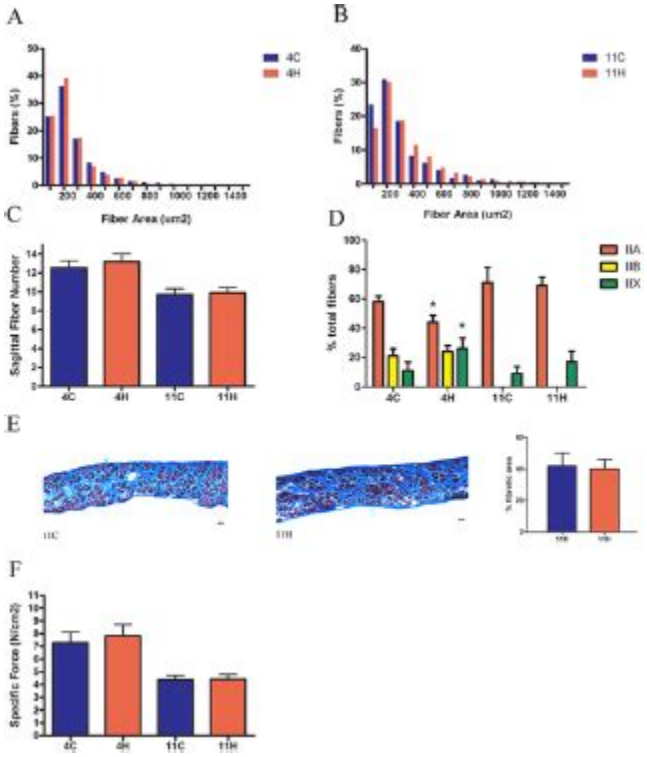
Hongyan Ren[1,5], Wei Xiao[1,5], Xingliang Qin[2], Gangzhi Cai[1], Hao Chen[1], Zaidong Hua[1], Cheng Cheng[2], Xinglei Li[3], Wenjun Hua[1], Hongwei Xiao[1], Liping Zhang[1], Jiali Dai[2], Xinmin Zheng[1], Zhe Zhu[1], Chong Qian[4], Jie Yao[2✉] & Yanzhen Bi[1✉]

Myostatin (MSTN), associated with the "double muscling" phenotype, affects muscle growth and fat deposition in animals, whereas how MSTN affects adipogenesis remains to be discovered. Here we show that MSTN can act through the MEF2C/miR222/SCD5 cascade to regulate fatty acid metabolism. We generated MSTN-knockout (KO) cloned Meishan pigs, which exhibits typical double muscling trait. We then sequenced transcriptome of subcutaneous fat tissues of wild-type (WT) and MSTN-KO pigs, and intersected the differentially expressed mRNAs and miRNAs to predict that stearoyl-CoA desaturase 5 (SCD5) is targeted by miR222. Transcription factor binding prediction showed that myogenic transcription factor 2C (MEF2C) potentially binds to the miR222 promoter. We hypothesized that MSTN-KO upregulates MEF2C and consequently increases the miR222 expression, which in turn targets SCD5 to suppress its translation. Biochemical, molecular and cellular experiments verified the existence of the cascade. This novel molecular pathway sheds light on new targets for genetic improvements in pigs.

[1] Key Laboratory of Animal Embryo Engineering and Molecular Breeding of Hubei Province, Institute of Animal Science and Veterinary Medicine, Hubei Academy of Agricultural Sciences, 430064 Wuhan, China. [2] Wuhan Bioje Biomedical and Technology Co., Ltd., 430000 Wuhan, China. [3] Wuhan Bioacme Biotechnology Co., Ltd., 430000 Wuhan, China. [4] Beijing Center for Physical and Chemical Analysis, 100094 Beijing, China. [5] These authors contributed equally: Hongyan Ren, Wei Xiao. ✉email: yaojie@biojust.cn; sukerbyz@126.com

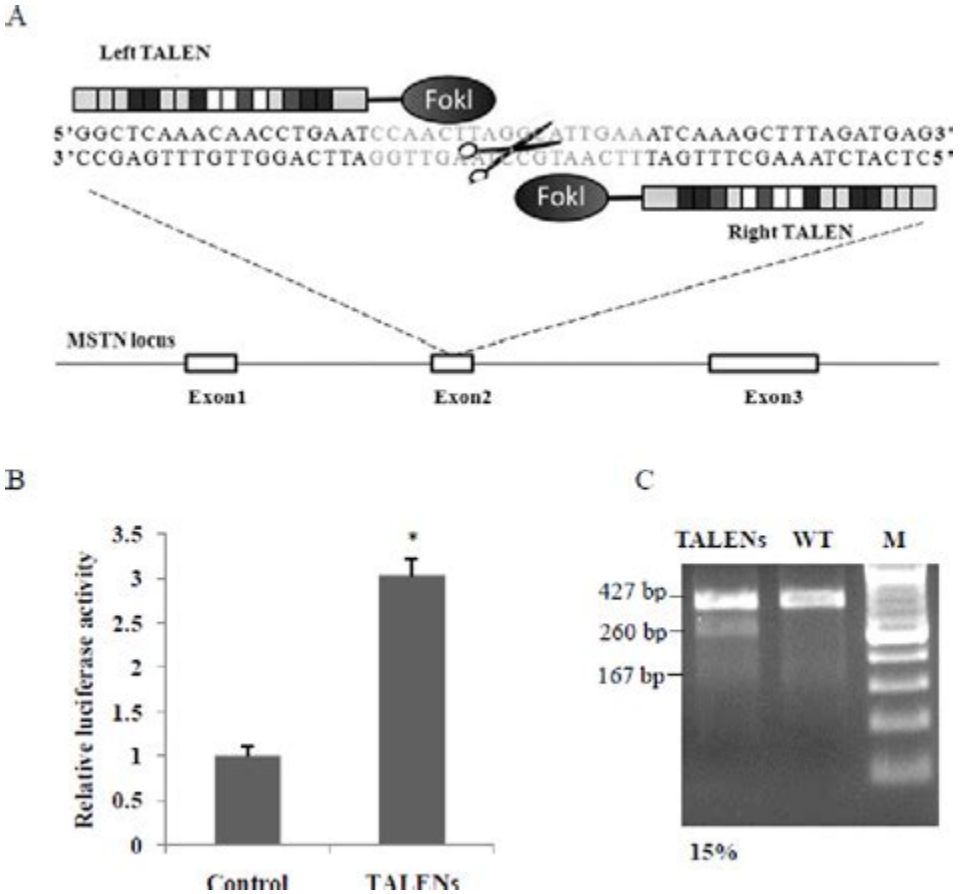
The application of new technologies for gene editing in horses may allow the generation of improved sportive individuals. Here, we aimed to knock out the myostatin gene (MSTN), a negative .

Long-Term Systemic Myostatin Inhibition via Liver-Targeted Gene .



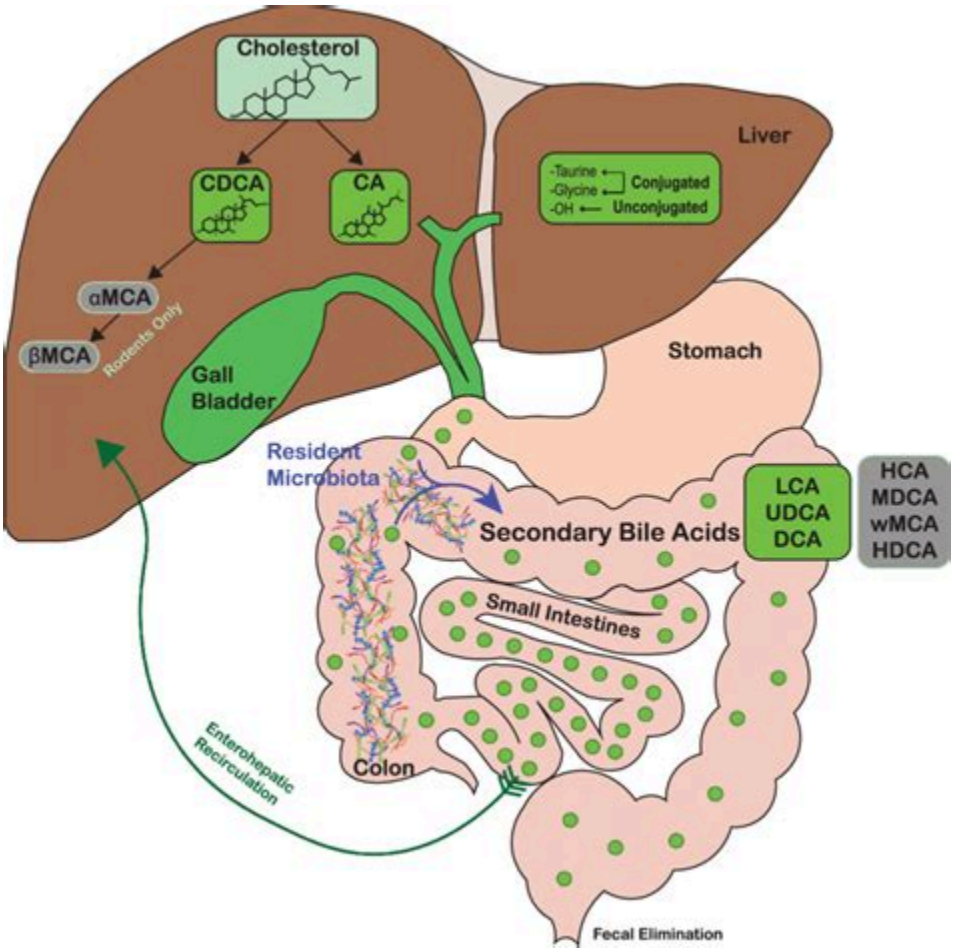
Myostatin (MSTN) gene knockout can increase lean muscle mass and has been widely used in livestock breeding. MSTN deficiency also regulates various metabolic processes. However, the effect of MSTN knockout on the liver, the largest metabolic organ, has not been reported.

Targeted Myostatin Gene Editing in Multiple Mammalian . - ScienceDirect



In the chicken DF1 cell line, we recently reported the efficient knockout system of myostatin gene with D10A-Cas9 nickase . gizzard, and liver. The quantity of abdominal fat mass except for intra-abdominal fat in the intestine was extracted and weighted from the sacrificed WT and MSTN KO chickens. . D10A-Cas9 nickase-based gene-editing .

Myostatin Knockout Regulates Bile Acid Metabolism by Promoting Bile .



Musunuru et al. 3 established a 63% base editing efficiency in the liver, which coincided with a mean 81% and 65% reduction of plasma PCSK9 and LDL cholesterol levels, respectively, all of which .

Myostatin is associated with the presence and development of . - PubMed

Myostatin (MSTN) is a transforming growth factor-β family member that plays a critical role in negatively regulating skeletal muscle mass. 1 Genetic studies have demonstrated that myostatin gene deficiency leads to muscle hypertrophy due to a combination of increased fiber numbers and increased

fiber sizes in multiple species including human, 2 .

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