# The potential of CRISPR to help lower mortality in bodybuilding

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## Abstract:

Bodybuilders often use anabolic androgen steroids to gain muscle but these substances are harmful to an individual's health as they cause unrestricted muscle growth. This unrestricted growth leads to an increase in cardiac muscle which can cause heart disease and death. Other hormone replicators, like human growth hormone, are also often used by bodybuilders and similarly promote uncontrolled muscle growth in the heart which can lead to death. I hypothesized that CRISPR technology could make the MSTN gene nonfunctional as an alternative treatment to hormone therapies for muscle growth. This approach would not promote global uncontrolled muscle growth, instead promoting skeletal muscle growth specifically. Gene therapy that inhibits muscle growth genes would benefit not only those trying to gain muscle but also those who suffer from various muscular degenerative health issues. However, gene editing carries significant uncontrollable risks, as there is a risk of off-target cutting which can lead to detrimental effects to one's health. Additionally, the cost associated with gene therapy is high.

## Introduction

Around 9.8% of gym users use anabolic androgen steroids (1). Anabolic androgen steroids (AAS) increase muscle growth in all muscle types, including cardiac, skeletal, and smooth muscle, when used with resistance-based training (2). However, AAS mimics natural sex hormones, like testosterone, which promotes harmful unrestricted muscle growth in organs such as the heart (2). This is bad as increased cardiac muscle mass has been found to increase mortality rates among users (3). Increased cardiac muscle mass puts strain on the blood vessels going into and out of the heart, which leads to various cardiac syndromes like myocardial dysfunction, cardiac arrhythmia, and sudden death (4). Additionally, AAS has a variety of other effects like a decrease in testicular volume and lower production of both sperm and testosterone due to inhibition of the pituitary gland (5). Overall, AAS are a dangerous class of hormones that cause an increase in the rate of mortality in bodybuilders. An alternative to AAS would be the use of human growth hormone (HGH) as it is another hormone that helps promote muscle growth. Alternatively, AAS could be replaced by CRISPR, a gene editing method, as the tool could render genes that inhibit muscle growth nonfunctional. While AAS and HGH are used to a wide degree for increasing muscle hypertrophy, gene editing technology is an unused resource to increase muscle hypertrophy.

## Discussion

*HGH is not a viable alternative treatment:*

Other options to increase muscle growth include human growth hormone (HGH), which increases skeletal muscle mass by replicating naturally occurring HGH (6). An increase in growth hormones does not decrease androgen levels or sperm production and instead induces joint pain due to rapid muscle growth and joint realignment (7). HGH, like AAS, promotes global muscle hypertrophy, in a similar fashion to AAS, which increases the mortality of athletes who use it (8).

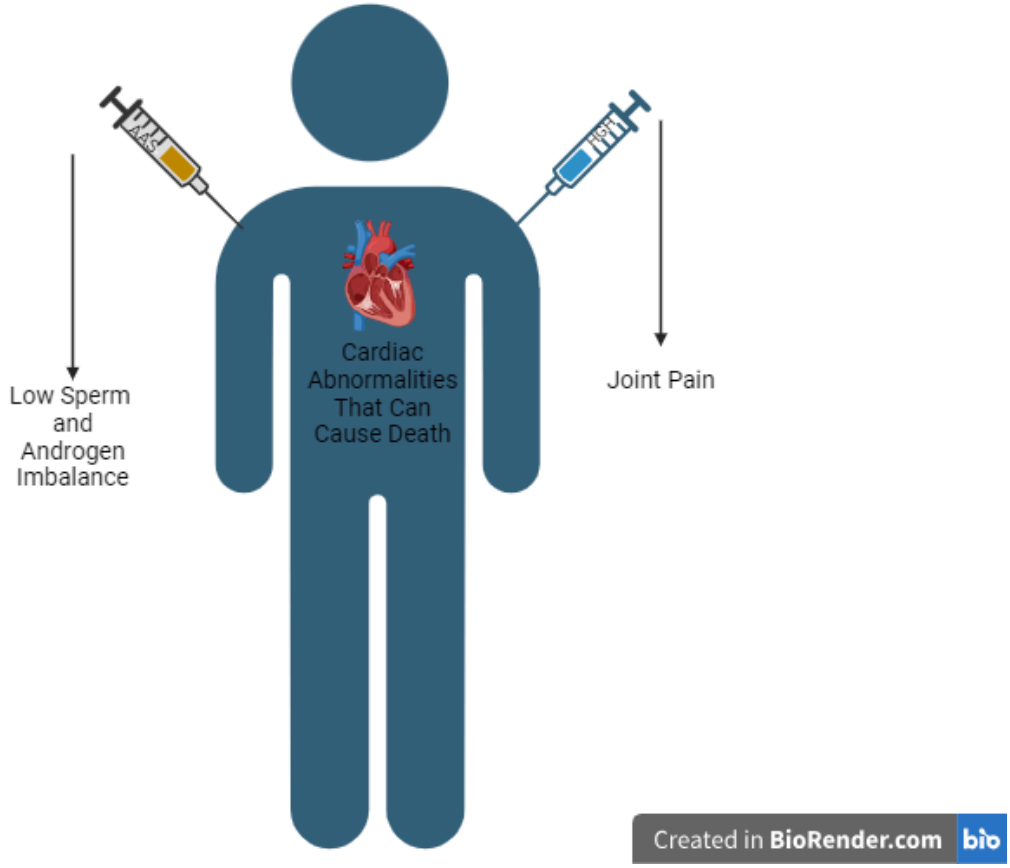


Figure 1: Side Effects of Injecting Steroids. The needles correspond to the 2 compounds HGH and AAS both of which an individual might inject into themselves to increase muscle hypertrophy. The arrows stemming from the needles and their corresponding text boxes show the adverse effects of their corresponding substances; with HGH or AAS.

The heart in the middle of the illustration was put there to indicate that both substances have negative impacts on the cardiovascular system. The corresponding text box then states those negative effects.
With both AAS and HGH causing individuals to have heart-based health problems, people are advised against using them. However, people still do use them, so it is important to consider alternative approaches, such as CRISPR, a gene editing technology.

*CRISPR and the Myostatin Gene:*
CRISPR is an accurate gene editing tool where an mRNA strand guides a Cas9 protein to a specific site in a genome sequence, which enables precise editing through the addition or deletion of specific genetic material. For gene editing to affect one's muscle mass a gene affecting one's muscle mass must be identified. One gene that controls muscle growth is called the Myostatin, MSTN, gene (9). The MSTN gene, when activated by working out, inhibits protein synthesis and reduces muscle hypertrophy overall. Additionally, this gene is exclusively expressed in skeletal muscle, meaning that inhibiting the gene does not promote global muscle growth. Inhibition of this gene would benefit bodybuilders as muscle growth would increase and there would be no effect on non-skeletal muscle (9). CRISPR technology targeting the MSTN gene could also help patients with muscular degenerative diseases similar to how it helps

athletes as patients could retain or even gain muscle mass, to combat muscle degenerative diseases.

*Side Effects of CRISPR Treatment:*
Nonfunctional versions of the MSTN gene occur naturally without negative side effects (10). However, the use of CRISPR in general is risky as its use could result in negative side effects. CRISPR could cause a frameshift change to the MSTN gene by either inserting or deleting genetic code. This would render the MSTN gene nonfunctional as the genetic code would be read by the RNA polymerase wrong thus creating abnormal proteins or a stop codon that would stop proteins from being produced in the first place. Both of these would result in the MSTN gene not being able to express itself.

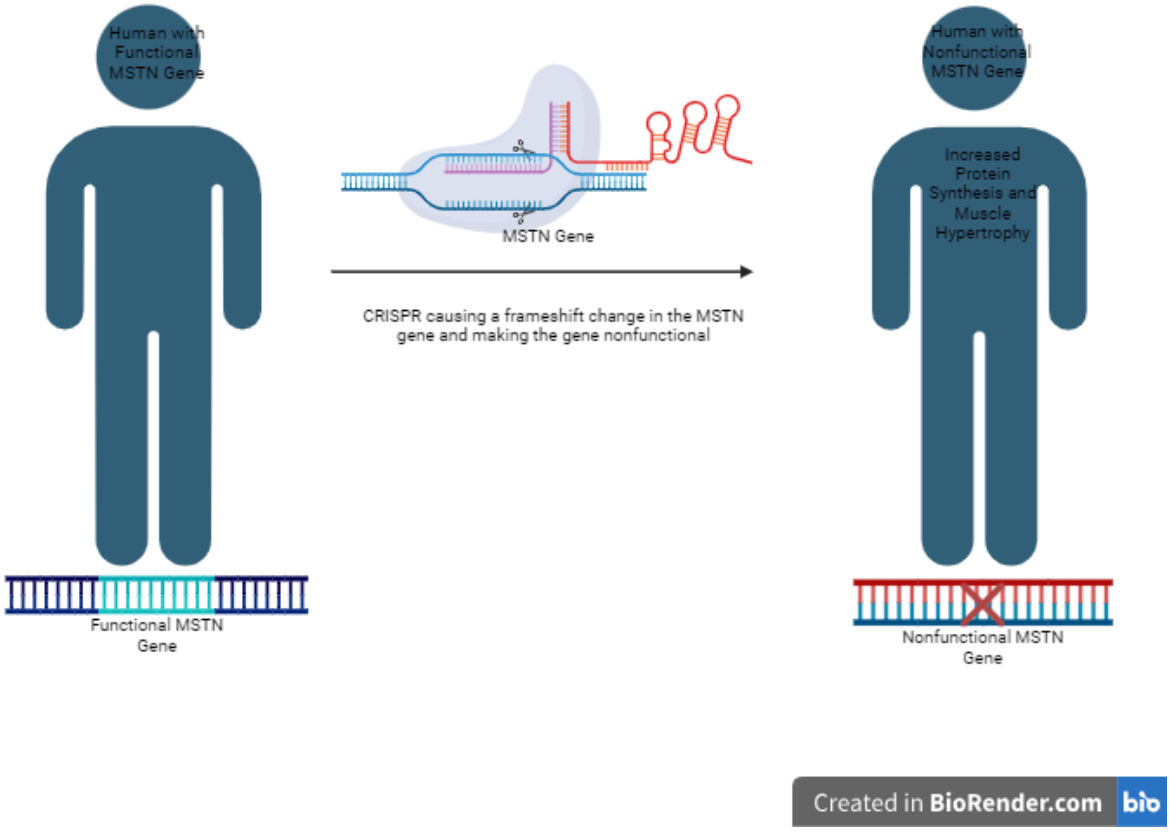


Figure 2: Myostatin Removal by CRISPR in an Individual. The arrow shows the use of CRISPR in an individual causing a frameshift change in the MSTN gene making it nonfunctional.
On the individual who is labeled with a nonfunctional MSTN gene the effects of CRISPR and the nonfunctional gene are listed on the torso with increased protein synthesis being stated. This results in the gene being nonfunctional.

CRISPR treatment comes at significant risk because it is not always predictable. Unfortunately, this treatment can result in unwanted gene changes, as CRISPR could cut out or insert genetic material into the wrong place due to technological error. These off-target cuts could affect any range of biological functions within an individual, depending on which gene is altered (11). While there are no direct negative effects of this treatment, there are substantial risks of off-target cutting and subsequent effects on gene expression. Being aware of such risks could

deter athletes and patients from seeking gene therapy. Another limiting factor of this treatment is the high cost (12). While using CRISPR to make the MSTN gene nonfunctional is a viable solution, with no direct negative side effects, the procedure to use CRISPR is expensive and could do irreversible harm to one's other bodily functions.

**Conclusion**

Overall, while individuals can and do use AAS and HGH to increase muscle hypertrophy, these methods are detrimental to their health. Instead, individuals could leverage gene therapy techniques, such as CRISPR, that would render their MSTN gene nonfunctional and eliminate some protein synthesis inhibitors thus increasing muscle hypertrophy. Additionally, there are few side effects of making the MSTN gene nonfunctional. Limitations to using CRISPR include cost and the willingness of athletes to receive gene therapy. To address the willingness of individuals to receive gene therapy, scientists could draw more attention to clinical trials showing the safety of gene editing. Cost however could be addressed by further investment in the gene editing field which would lead to development and a decrease in the cost of procedures. CRISPR, the gene editing tool, is a healthier substitute to HGH and AAS when concerning muscle hypertrophy.

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