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Review Article

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Genetic Manipulation to Improve Athletes Performance - A Critical Review

D S R S Prakash

Department of Biotechnology, Adikavi Nannaya University, Rajamahendravaram-533 296, East Godavari District, Andhra Pradesh, India

*Corresponding author
D S R S Prakash, Department of Biotechnology, Adikavi Nannaya University, Rajamahendravaram-533 296, East Godavari District, Andhra Pradesh, India.

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Abstract

Genetic manipulation as the name suggests is the modification of genes. It is the process of changing the structure of the genes of a living thing in order to make it healthier, stronger, or more useful. It is the direct manipulation of an organism's genes using biotechnology used to change the genetic makeup of cells including transfer of genes. The need of genetic modification is to enhance the performance of particular genes, this method is implemented effectively to enhance the quality of food, fight various chronic diseases like cancer, cloning etc. However, this paper is limited to the use of genetic manipulation to enhance Athletics performance of the athletes and healing process of the cells. There are various contradictory thoughts over the use of genetic manipulation in Athletics over its use being ethical or unethical. There have been various normative arguments both in favor and against its use in Athletics. However, no competent authority has prohibited its use in Athletics. There are various methods involved in gene modification, few prominent are discussed in this paper. Genetic manipulation, the process of inducing changes in gene expression and the expression of novel genes, has proven to be an indispensable tool in recent genetic research. The implementation of increasingly powerful genetic tools to mouse embryonic stem (ES) cells has led to an explosion of data concerning the specific properties of an extremely large array of genes. Current available techniques allow for the specific elimination of target gene expression, tissue specific induction of reporter gene expression, the over expression of cellular genes, and more. It is not surprising, therefore, that a short time after the derivation of human ES cells, several studies describing genetic manipulation of these cells have been reported. This focuses on the recent advances in the genetic manipulation of human ES cells, the methods currently available, and their possible utilization. A brief discussion of advanced genetic manipulation techniques not yet demonstrated in these cells is also presented. Through this paper the author has tried to summarize various methods, aspects, approaches and arguments involved with genetic modification in Athletic persons.

Keywords: Athletes, Genetic Manipulation, Gene Transfer Techniques.

Introduction

Genetic manipulation or modification is the act of modifying genetic makeup of an organism. It is the direct manipulation of the genome using molecular engineering techniques. Manipulation can be generated by methods such as gene targeting, nuclear transplantation, transfection of synthetic chromosomes or viral insertion [1]. Genes are the working subunits of DNA. Each gene contains a particular set of instructions, usually coding for a particular protein or for a particular function [2].

Human genetic modification is the direct manipulation of the genome using molecular engineering techniques. Recently developed techniques for modifying genes are often called "gene editing." Genetic modification can be applied in two very different ways: somatic genetic modification and germline genetic modification.

Somatic genetic modification adds, cuts, or changes the genes in

some of the cells of an existing person, typically to alleviate a medical condition. These gene therapy techniques are approaching clinical practice, but only for a few conditions, and at a very high cost.

Germline genetic modification would change the genes in eggs, sperm, or early embryos. Often referred to as "inheritable genetic modification" or "gene editing for reproduction," these alterations would appear in every cell of the person who developed from that gamete or embryo, and also in all subsequent generations.
For safety, ethical, and social reasons, there is broad agreement among many scientists, ethicists, policymakers, and the public that germline editing is a red line that should not be crossed. Using germline editing for reproduction is prohibited by law in more than 40 countries and by a binding international treaty of the Council of Europe. However, in November 2108, a scientist named He Jiankui announced he had edited the genes of twin baby girls who had subsequently been brought to term. His reckless experimentation has been nearly universally condemned. This development has sparked new debate around human germline modification, particularly between parties who desire to push the technology forward and those who fear it could open the door to a new market-based form of eugenics. An organism that initiate through genetic engineering is considered to be genetically modified (GM) and the resulting entity is a genetically modified organism (GMO). The 1st GMO was a bacterium prompt by Herbert Boyer and Stanley Cohen in 1973. Rudolf Jaenisch fabricated the first GM animal when he loaded foreign DNA within a mouse in 1974. The first company to focus on genetic engineering, Genentech, was founded in 1976 and started the production of human proteins [3].

How Does Genetic Modification Work?

Genetic modification is the technique of inserting well functioning genes into cells in order to correct a genetic error in those cells, or to introduce a new function to the cells. This technique used to be called 'gene therapy' but the preferred terminology at the moment is 'genetic transfer technology', because it is not clear that modifications will be therapeutic in all cases [4].

Genetic modification can take place in various ways and has made progression since the science has become more refined.

The various ways are appended below:

Biolistic or Particle Gun Method

This method involves mixing of DNA with tiny metal particles, and is then fired into a tissue culture of cells or into an organism itself. For some time it was believed that the best of introducing new genes into cells might be to simply blast them using a biolistic or particle gun.It has been noted that this method has not been very effective, as it may damage the cells and it is not very successful at promoting the update of foreign DNA. It is also possible to transmit the genetic material by injecting it in the organism. This ensures a better uptake of foreign DNA [5].

Vector Method

A completely different method is by using some kind of vehicle, named a vector, to transfer the genetic material into human cells and tissues. A vector is an organism that carries genetic material from one species (the donor species), and finally injecting the species (carrying the new genetic material) into the host. To make this even more efficient, DNA can be wrapped into a virus particle, while having the dangerous parts of the virus have been disabled through genetic modification. This way the harmful virus genes are removed and replaced by donor gene [6].

After injection with the viral vector, the virus will begin infecting the cells with the new DNA, and in that way it will be transferred throughout the organism. These vectors have been constructed from different kind of viruses, including potentially dangerous viruses like the human immunodeficiency virus (HIV), herpes virus, pox viruses or cancer causing mouse leukemia viruses. In all cases the dangerous genes of these were removed or deactivated, which gave the virus only one function: act as a "Trojan horse" and sneaks the foreign genes into the organism cells [7].

Electroporation

Another vector less method involves electroporation. In this method, the cells that are to be genetically engineered are placed in a solution of foreign DNA and applying a high voltage electric field then stimulates the integration of the new genetic material into host cells. Electroporation is carried out with electro orators, purpose- built appliances which produces an electrostatic field in a cell solution. The cell suspension is pipetted into a glass or plastic pot that has two aluminum electrodes on its sides. For bacterial electroporation, commonly a suspension of around 50 microliters is used. The cell membrane is unable to pass current (except in ion channels), it works as an electrical capacitor. Exposing membranes to a high-voltage electric field effects in their interim breakdown, resulting in pores which are large enough to let macromolecules (such as DNA) to come inside or leave the cell. The accomplishment of vivo electroporation rely heavily on voltage, iteration, pulses, and timing. Developing central nervous systems are most effective for in vivo electroporation because of the discernibility of ventricles to inject nucleic acids, as well as the increased permeability of parting the cells [7].

What Kind of Genes Are Being Modified?

Some commentators have raised concerns that genetic modification or "gene doping" will be the next step in the search for enhanced performance [9-11]. These concerns are based on some impressive studies in genetically modified rodents where manipulation of individual genes has increased muscle mass, muscle strength, or running endurance, depending on the gene that was manipulated. Reviews of these animal studies conclude that such genetic manipulations could also improve human athletic performance [12, 13].

How likely is it that athletes will use genetic modification? About 10% of athletes have used existing drugs, so it is likely that some will be tempted to experiment with genetic modification [14]. However, translating studies performed in rodents into effective treatments in humans will not be easy. Some of the rodent studies were performed in transgenic mice in which the genetic modification was introduced into the germline and transmitted from one generation to the next. For practical and ethical reasons, it is not possible to do this in humans.

Widespread genetic modification of somatic rather than germline tissues can be achieved in mice by using modified viruses to deliver the genetic modification, but only when used at very high doses. Scaling up such doses from a 25 g mouse to a 75 kg human will prove challenging, both in terms of the facilities needed to generate such viral vectors and the potential difference in immune responses

to such viruses between mice and humans. It is also not known how well these vectors will work in humans.

Current clinical trials-for example, those targeted at muscular dystrophies—use only small amounts of these viral vectors, and they are early stage safety trials that will not tell us whether we can achieve the high efficiencies needed to improve muscle function [15]. It will be many years before agents for gene therapy are available for general clinical use.

The known genes that can improve athletic performance are very few. To make it medically relevant, a lot of basic scientific research is required to be done and it just also may have a more sinister application in athletic performance. One gene that worked in mice to conceive a so called "marathon-mice" is a gene called PPAR delta. It was introduced in mice in 2004 and allowed them to increase their Type I and Type II muscle fibers which means they could run two times as far as their litter-mates-an obvious advantage for anyone in endurance Athletics.

There's also IGF-1 (insulin-like growth factor 1), a gene that could be modified and used to help to heal the muscles. It was first introduced in gene therapy in a mouse to try to cure Duchenne's muscular dystrophy and also helped mice maintain muscle tone and fitness into old age [16].

Athletics Gene Enhancement On the Horizon?

Is it ethical, for example, for an athlete if he uses genetic therapy to repair his body if he has been injured himself after super-aggressive training and attain an advantage over other competitors who were more judicious in their training program? What for the athletes who use genetic modification to bridle a debilitating disease-and also realize a side benefit of improved performance? Should they be banned from the competition or only from some kinds of competition? And beyond winning and losing, of course, athletes health is the largest issue. The use of genetic amplification may pose health hazards, many of them still unknown and some of which may never be known [17].

To be sure, there are some concerns about genetic enhancement in Athletics which are overblown and, despite dramatic innovations such as CRISPR gene editing is still futuristic. So-called designer babies, for example, are science fiction, although recent progress suggest the future may be nearer than we think. Although some start-up companies have tinkered with the idea, it may be a decade or more before scientists can remove embryonic fluid or swab your genes and create a readout of the expected sporting accomplishments of our prodigies in waiting [18].

Less distant are gene therapies and gene editing, proved earlier on animals, that if transferable to humans it might be able to regulate energy metabolism, alter blood flow to the tissues, modify pain perception, or even delay sexual development to keep preadolescent females-perhaps gymnasts and figure skaters of the future-in their performance prime. There are many of active studies involving human clinical trials, with various therapies seeking federal approval. Scientists and athlete's guinea pigs are also busy trying out gene enhancements to recapitulate the body after cartilage damage, tears and fractures.

Synthetic drugs which are used to boost endurance or increase strength and speed are already widely available. Grounded to international cycling and weightlifting only a few years ago, gene doping invaded winter Athletics, track and field, the NFL and even World Cup soccer. And even after new screening measures it has curtailed the practice, many people suspect that the problems remain. World sporting organizations, the Olympic movement and world cycling in particular, have been proved unlucky over the years in screening for dopers [19].

The genetic turnover will be even more challenging. Hostile classic drugs like steroids and bioengineered substances or body tweaks that are chemically identic to the body's natural hormones, makes detection very difficult. The issues will be increasing exponentially in the next era of genetic enhancement, the direct injection of viruses or different delivery agents that carries DNA which can formulate genes into the energy factories or activate dormant muscles. "If direct injection will be applied, the DNA will only be present in that particular muscle," noted that Peter Schjerling of the Copenhagen University Institute for Athletics Medicine.

"A positive test would need coring out of actual muscle tissue. Not many athletes would be allowing that. And the sample need to be taken at the exact spot of the injection." Certainly genetic modification is becoming more and more attractive option for those who are inclined to cheat in competitions because it cannot be virtually detected" said Charles Yesalis, a Penn State University Athletics scientist and world expert on performance improving drugs. "If things would spin out of control, it could be a freak show in athletics" [20].

Genetic modification is an issue, whether in stem cell research or GMOs, which stirs an immediate and powerful gut reaction. In recent few years, biomedical researchers have made a small but measurable changes in developing bio-engineered drugs. Many looked forward, perhaps unrealistically, to an age where many diseases will be wiped out and hospitals will be obsolete except to treat trauma. But if such a revolution occurs, invariably it would result in collateral damage [21].

Normative Arguments of Genetic Modification in Sport

Genetic modification in sport has build a large scale of discussion on ethical implications. Research has been published with normative arguments that are both in favor and against this relatively new technology.

Normative Arguments in Against of Genetic Modification in Sport

Some arguments to refuse the approval of the progression of genetic enhancement technology in sport for practical, health, and ethical reasons have been presented. From a practical viewpoint, there is not a concrete ideal athletic body type. For example, ideal boxers have different built than ideal hurdlers. The fact that ideal body types differs depending on the sport is uncertain because germ line modification requires that genetic choices should be made prior to birth. Parents, in effect, will have to predict as to what sport the child would be interested in the later life. If a child is born with expectations to become an elite swimmer because he or she was "built that way," it creates ethical issues regarding the individual's right to be able to make their own choices. In addition, Sherwin warned that genes are not fate; there are environmental factors also that influence the success and failure in Athletics. Therefore, gene

therapy is not a full proof method which guarantees to link directly to athletic success [22].

Genetic engineering is a very risky procedure when it comes to overall health. Preliminary tests on gene modification had been unpredictable, and there is still a lack of surety as to how a body will respond to a gene therapy. In fact, testing in this field had resulted in unfortunate tragedies in some cases. An example of this is the case of Jesse Gelsinger, an 18-year-old student who became a subject for clinical research on gene therapy. His body did not respond well to the therapy, and as a result he died within 96 hours of the treatment. Not all clinical trials have ended in this tragic manner, but safety is still a cause for concern [23].

Apart from risk and practicality, there are many other objections against the use of gene doping or genetic modification in sport. One thing to worry is that the use of this technology could result in unexpected consequences. Genetic modification could change sport, as we know it in significant and permanent ways. The new class of humans that would result from germ line enhancement would encounter with unenhanced persons in sport, therefore it creates a potential disadvantage for the unmodified. This would create a state of inequity and questioning on the fairness of sport, as not all the athletes would have access to the technology because of its price, availability, or other factors. If it follows, then, to be just in sport, different classes would be formed, like weight classes in boxing or wrestling. In this case, the two class choices would be modified athletes and unmodified athletes. Whether the idea of classes would be accepted or not is yet to be seen. However, the idea of different classes has a major drawback. Division of such classes would detract from the sole purpose of gene doping or genetic modification, which is to attain some sort of an advantage. Fairness has always been a key subject of ethical discussion in sport, and genetic modification for performance enhancement in sport gives a new dimension to the topic [24].

An additional normative argument against the usage of gene modification for sport purposes rotates around the issue of privacy. If genetic modification becomes widespread and is acceptable in sport, protocols regarding privacy of personal information, especially DNA, would need to be established. Genetic engineering needs testing of genes and DNA. The information obtained from the testing would identify "all the processes that occurs in the body and can be used to estimate the chances of disease, or even to define a particular type of human character". Due to the disclosing nature of the information ascertained from the tests, there would be a sure need for privacy regulations.

Elaborating beyond sport, the lack of privacy in the matter could lead to genetic distinction from life or health insurance companies, as information give on any individual's genotype could be accessed. Putting safeguards in place to avoid this type of discrimination from occurring is a necessity. In this age of technology, the skill to collect, share, and manipulate personal information through computers has given some difficulties in maintaining privacy for individuals. There is valid concern about privacy that needs to be resolved before genetic engineering can be become an acceptable practice in sport [25].

Normative Arguments in Favor of Genetic Manipulation in Athletes

Research also exists that promotes the idea of genetic Manipulation in athletics. One such argument is that genetically manipulated athletes would perform at higher, unimagined levels, which will add more excitement to sport. As a result, fan base and attendance at sporting events will potentially grow. Since physique would be predetermined by genetic modification, the results of sport competitions in the future will be based more on psychological, moral, and intellectual strength, thereby making the competitions purer. For example, as it stands today, basketball players do vary in height, with the taller players particularly having a major advantage. If genetic technology is used in such a way so that all players are tall, the physical advantage will be negligible, and constitutive game skills, combined with mental toughness, will determine which competitors will win [26].

To counter the argument that genetic engineering could potentially cause major health issues, it has been mentioned that people have always devised ways in which to enhance or improve their physical condition. While genetic technology has inherent risks today, other technologies were also considered risky when first introduced. For example, certain weight training techniques and special dietary regimes can be risky for individuals, but they are still permitted as methods of performance enhancement in sport [27].

It has also been speculated that genetic technology has societal and sport-related benefits. Brown suggested that there is a responsibility to use scientific knowledge which will improve physical wellbeing. It is impossible to see into the future, though, so there is no definite way of assuming the actual benefits or harms of using genetic technology for enhancement in performance. However, just keeping the status for the very sole purpose of fearing risk or change which does not allow for improvement. "We can only brawl to make things better for ourselves and our children as best as we can, knowing that we will often fail in these efforts, and are dimly aware of our next steps and their uncertain directions". Brown's arguments are crucial ones that demonstrates the need to critically evaluate change and consider an improvement that result from it [28].

While many ethicists and theorists have labeled genetic modification an unfair process, there are some who disagree. Loland asserted that as long as the safety provisions and equal access opportunities are put in place, revolution in sport technology should be pursued as methods of bringing out athletic talent and overall human excellence. Loland's argument assumes a state of equity. However, due to the "genetic lottery" of life, it could be actually considered unfair to not utilize the technologies of genetic modification. It is a reality that inequality exists in various facets of life. For example, life is often considered unfair for individuals who have the lack of resources to overcome economic or social disadvantages. Similarly, it could be argued that genetic differences in individuals also lead to inequity of resources or opportunities. Thinking along these lines, Fox contended that the use of biotechnology and genetic manipulation has the potential to move us towards a more just society. Fox, like most proponents of genetic engineering, is also aware of all the ethical concerns involved and recommends a cautious approach for implementation of this new technology [29].

Conclusions

If genetic manipulation or modification is permitted as a means of performance enhancement, elite sport will most certainly have a new look with new concerns. Though research is limited and is inconclusive at this time, there is preliminary consensus that genetically modified athletes would have some type of advantages

over those who are not the products of genetic technology. In elite sport, that advantage, even if it is too small, could be a difference maker in close competitions. Because physical attributes of genetically modified athletes will not be as necessary to develop, extra attention will need to be placed on psychological training, with more emphasis on motivation and focus. Elite sport and competitions could potentially become more exciting and showcase more highly developed athletes as a result of this new technology if permitted.

Human genetic modification is the direct manipulation of the genome using molecular engineering techniques. Germline genetic modification would change the genes in eggs, sperm, or early embryos. Genetic engineering is the process of using recombinant DNA (rDNA) technology to alter the genetic makeup of an organism. Traditionally, humans have manipulated genomes indirectly by controlling breeding and selecting offspring with desired traits.

As indicated by the research, a concentrated effort should be made on measuring the pros and cons of genetic manipulation. This can only happen through additional study, intense research and discussion. Athletics leaders and policy makers will have to settle the debate and determine that what types of genetic manipulation, if any, will it be acceptable for sport. Whatever the end result may be, it is clear that, the sport is continuously growing and ethical issues will continue to surface as athletes search for the latest and advanced methods of enhancing performance.

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