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## **CRISPR therapy - revolution in medicine or ethical danger**

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## **Abstract**

CRISPR, or rather rarely used full name – *Clustered Regularly Interspaced Short Palindromic Repeats*. Studying this family of DNA sequences has led to the creation of CRISPR-Cas9 technology for genome editing. This technology has been with us for quite some time and is undeniably considered one of the most significant breakthroughs in modern genetics. It provides a powerful weapon for editing genomes with unprecedented precision, which can be used for advancing biotechnological inventions, finding and deploying new treatments and for overall progress in medicine. Recently, spikes of progress have been seen, which unquestionably have sparked many ethical and moral discussions about this technology. This paper examines the revolutionary potential of CRISPR therapy in medicine, alongside the ethical and moral implications that arise from its application. The potential of the therapy has been placed in a specialised context – how the implementation of CRISPR-Cas9 could impact sportsmen and -women, especially those battling such hard genetic diseases as Paralympians in different disciplines do every day. By analysing the scientific advancements, potential applications, and ethical dilemmas, a comprehensive understanding of CRISPR's impact on contemporary medicine and contemporary sports is developed.

**Keywords:** CRISPR, clustered regularly interspaced short palindromic repeats, CRISPR-Cas9, ethical implications, moral challenges, genetics, modern genetics, innovative medicine, progressive medicine.

## **I. Introduction**

Humans are part of a living ecosystem that consists of thousands of genes. Genes that are a complicated system of constant '*recombination, replication, repair, division, differentiation, progression, and inheritance*'.<sup>1</sup> Genes that for the last few years have been under the loop of studies of many researchers – revolutionising the field by groundbreaking findings and milestones such as nucleic acids (DNA, RNA) identification, polymerase chain reaction and most concerning for this thesis – biological scissors (CRISPR-Cas9). There is no doubt that the CRISPR-Cas9 discovery has revolutionised molecular biology and, consequently, medical studies, as it enabled manipulations of genes at a level of precision unseen before. Moreover,

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<sup>1</sup> Swati Tyagi et al., '*CRISPR-Cas9 system: A genome-editing tool with endless possibilities*' (2020) Journal of Biotechnology 319, 36–53, p 36.

this technology is not only restricted to humans but can act upon diverse organisms, which makes the scope of its use significantly broader. As can be deduced, having the power to enter the genome and according to alter it to our needs holds the promise for treating various genetic diseases, advancing agricultural practices, and offering insights into complex biological processes – all of which may offer a positive impact on sports.

Nevertheless, alongside these potential medical benefits, there is a daunting side to this *hope for the future*. CRISPR came into the world of science with inherently attached ethical questions that necessitate thoughtful examination before employing this technology. Such an argument holds especially valid in current, new trends emerging of combining the CRISPR technology with artificial intelligence (AI) – both of which are under scrutiny for their actual value and protection of the human element in the equation.<sup>2</sup> This is only one example of how ethically questionable CRISPR may seem to some. Hence, there is a need to firstly examine what CRISPR technology is and accordingly what it entails (**Section II**). Next, this article will elaborate on the potential the technology holds, specifically for medicine (with an emphasis on medicine in sports, **Section III**). This will be followed by laying down what most pressing ethical considerations accompany CRISPR and those that are considered relevant for this paper (**Section IV**). Some of the challenging ethical considerations specific to sports will be assessed. Along these lines, this paper will turn to briefly assessing how dealing with CRISPR-Cas9 by enacting relevant regulation works. Finally, the findings will be neatly summarised in the conclusion (**Section V**). Ultimately, this paper aims to evaluate whether CRISPR is considered a revolutionary advancement in medicine and sports or a source of potential ethical danger.

## II. Overview of CRISPR Technology

CRISPR technology is based on a natural defence mechanism in bacteria that protects them from viral infections. More specifically, as accurately and neatly described by Swati in his work, it is ‘an RNA-mediated, sequence-specific adaptive immunity in prokaryotes that protects from bacteriophages and viruses’.<sup>3</sup> It acts as molecular scissors by separating several repeats (20-50 bp long) with spacers of resembling length and under CRISPR proteins. The whole process involves three vital phases: adaptation, biogenesis and identifying and degrading the foreign DNA. The first part is the part where the viral genome is recognised with viral attack, and, acting as a spacer, it is transferred into the CRISPR array. The second phase involves this array being transliterated into pre-CRISPR-RNA (also known as crRNA), and processed to form mature crRNA. The last step of degrading DNA completes the whole cycle as it brings the foreign DNA to meet the standard of these crRNA, which would otherwise be impossible of absorption due to the protection of the bacterial cell.

In simple terms, the technology utilises RNA sequences associated with the Cas9 protein to identify and cut specific DNA sequences within a genome. This ability to cut and edit DNA has applications in various fields, including medicine, agriculture, and biotechnology. Even though, at a theoretical level, it could be expected that these processes would require high-precision equipment and a sophisticated laboratory setting, it can look no different, as no extravagant machineries are needed.<sup>4</sup> What you will essentially need is a guide RNA sequence (20-30 bp long) and Cas9 nuclease. This makes this method rather financially beneficial, as there are many

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<sup>2</sup> Bhat A. Ajaz et al., ‘Integration of CRISPR/Cas9 with artificial intelligence for improved cancer therapeutics’ (2022) *Journal of Translational Medicine* 20(1), 1–18.

<sup>3</sup> *Supra* note 1 at p 36.

<sup>4</sup> *Ibid* at p 37.

other technologies that are so advanced in their needs that most of the laboratories are not able to work on their development. This is not the case with CRISPR-Cas9. One of the fundamental findings of the technology was that it may be used not only in a test tube but also within a nucleus of a living cell by locking onto a short sequence known as PAM (*Protospacer Adjacent Motif*).<sup>5</sup>

As recognised by Yuan-Chuan Chen in his work, the technology has already been variously studied, and nowadays, the topic revolves around different types of CRISPR-Cas9 systems, such as conventional systems and emerging systems for genome and transcriptome modification.<sup>6</sup> The latter has been adapted for the purposes of conducting ‘large economic deletions, large economic insertions into safe harbour loci, which remains somewhat challenging using conventional CRISPR-Cas systems’.<sup>7</sup>

### III. Applications in Medicine and Sports

As CRISPR technology is not limited in its use only to one gene but may act upon multiple genes, it is extremely relevant for medical studies as it has the ability to bring innovative treatments for diseases for which a combination of genes is responsible.<sup>8</sup> This was something discussed earlier, and also noted by Araldi Rodrigo Pinheiro, who in his work disserted on gene-editing technologies such as meganucleases, ZFNs, and TALENs, which present significant limitations compared to CRISPR.<sup>9</sup> Additionally, as previously briefly noted, CRISPR is described as an adaptive immune system in bacteria and archaea, which is naturally used for defence against viruses and plasmids, which brings the needed flexibility and adaptability of the technique to be used within a variety of genes.<sup>10</sup>

Consequently, there has been a lot of potential seen in this innovatory method in gene therapy for correcting genetic diseases by precisely targeting the ‘fruits of the poisonous apples’ in the codes – i.e. the component that is responsible for the genetic disease.<sup>11</sup> However, this is not always a clear-cut case, as it is not always an easy task to identify with a high certainty such clear causes of diseases. Especially, considering two factors – firstly, it is always difficult, if not impossible, to predict with certainty in medicine. Secondly, there are still some diseases that are constantly being investigated, and new information emerges timely. Such numerous genetic disorders, to name a few, may be sickle cell anaemia, cystic fibrosis, and muscular dystrophy. Studies have shown success in using CRISPR to edit genes responsible for these conditions in laboratory settings and animal models.<sup>12</sup> However, the practical applicability, based on these theoretical high expectations, is yet to be unravelled.

On another spectrum, the technology has been applied to creating genetically modified immune cells to target cancer more effectively. Furthermore, using iPSCs in regenerative medicine and in oncology enabled identifying drug targets and developing immunotherapies in

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<sup>5</sup> Rodrigo Pinheiro Araldi et al., ‘Medical applications of clustered regularly interspaced short palindromic repeats (CRISPR/Cas) tool: A comprehensive overview’ (2020) *Gene* 745, p 3.

<sup>6</sup> Yuan-Chuan Chen, ‘CRISPR technology : recent advances’ (IntechOpen, 2023), pp 13-26.

<sup>7</sup> *Supra* note 6 at p 17.

<sup>8</sup> Arif N. Ansori et al., ‘Application of CRISPR-Cas9 genome editing technology in various fields: A review’ (2023) *Narra J* 3(2), e184, pp 4-10.

<sup>9</sup> *Supra* note 5 at p 2.

<sup>10</sup> *Ibid.*

<sup>11</sup> *Ibid* at p 9-10.

<sup>12</sup> *Supra* note 5 at p 11 and Eva Vermersch et al., ‘CRISPR/Cas9 gene-editing strategies in cardiovascular cells’ (2020) *Cardiovascular Research* 116(5), 894–90 , p 889-900.

a much more predictable and safer manner, with potential that could not have been unlocked prior to the use of CRISPR.<sup>13</sup> This involves using CRISPR to deactivate viral pathogens (like HPV and HBV), which are concomitant with cancers. In clinical trials, CRISPR therapy has demonstrated promise. For instance, as also mentioned priorly, a recent study reported the successful treatment of sickle cell disease using CRISPR-Cas9 technology, where patients showed significant improvement in symptoms and increased production of healthy red blood cells.<sup>14</sup> We can imagine the positive impact such improvements could also have on those struggling with this disease in sports. Additionally, more people who are sick and have abided by physical activity would no longer be bound to do so. However, again, most of the actual trials were based on the so-called *animal models*.<sup>15</sup> This means that they are based on studying humans and human diseases through the lens of trials on animals such as mice and zebrafish. As a result, it is not known what effect the technology will have on humans, as it has with other sectors of medicine.

Nevertheless, the advancement emphasises CRISPR's potential as a viable therapeutic option compared to traditional gene therapy methods. If the technology could really work on humans and the expectations from the *animal models* could be transposed at least in the slightest bit, then CRISPR would offer even more valuable insight than has been given to the world of science regarding genetics. As could have been observed, there is a lot that CRISPR technology has to offer, which partially stems from the variety of things it might be used for. Moreover, it is still unknown if the options of CRISPR applicability that are available now will not soon have an even broader scope. This remains to be seen. Simultaneously with the constant progress made in the method itself, the growing concerns – especially those of an ethical nature – have been raised. Hence, there is a need to investigate those.

## **1. CRISPR-Cas 9 and Athletic Performance: Targeting Implications for Sports Medicine**

Having observed the above implications of CRISPR-Cas9 technology, it is logical to reach a hypothesis that the potential applications of the technology extend beyond conventional medical treatments and could also encompass the field of sports medicine, particularly for athletes with genetic conditions (not only sickle cell disease, which was previously noted). Paralympic athletes, who compete despite various physical impairments – many of which have genetic origins – constitute a distinctive population that could potentially derive benefits from CRISPR therapy in the future.

Genetic disorders impacting athletic performance include muscular dystrophies, metabolic disorders, and conditions affecting cardiovascular function. For instance, athletes suffering from Duchenne muscular dystrophy or limb-girdle muscular dystrophy face progressive muscle weakness that severely hampers their competitive capabilities.<sup>16</sup> CRISPR-Cas9 could, in theory, target the dystrophin gene mutations responsible for these conditions, potentially restoring muscle function and enabling these athletes to compete more effectively. Similarly, athletes with sickle cell disease may encounter complications during intense physical exertion. The

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<sup>13</sup> *Supra* note 5 at p 10.

<sup>14</sup> So Hyun Park and Bao Gang, 'CRISPR/Cas9 gene editing for curing sickle cell disease' (2021) *Transfusion and apheresis science* 60(1), 1-18, p 1-4.

<sup>15</sup> *Supra* note 5 at p 11.

<sup>16</sup> Ines Vandekerckhove et al., *Muscle weakness but also contractures contribute to the progressive gait pathology in children with Duchenne muscular dystrophy: A simulation study* (2025) *J Neuroeng Rehabil.* 22(1), 103.

successful treatment of sickle cell disease utilising CRISPR-Cas9, as previously mentioned, suggests that athletic populations carrying this trait could benefit from gene therapy interventions aimed at enhancing their performance capacity while concurrently addressing health concerns.

However, beyond therapeutic applications for genetic disorders, CRISPR technology raises substantial ethical and practical questions regarding performance enhancement in sports. Those are linear to using it in medicine generally. Here, another layer may be added, as the technology could theoretically be employed to modify genes associated with muscle growth (such as the myostatin gene), oxygen utilisation (EPO gene), or fast-twitch muscle fibre development, which in turn would not constitute just treating a sick patient. This potential form of “*genetic*

| System       | Source                        | Mechanism  | Advantages   | Limitations  |
|--------------|-------------------------------|--|--|--|
| CRISPR-Cas9  | <i>Streptococcus pyogenes</i> | Cas9 pairs with a sgRNA to introduce a DNA DSB 3 nt upstream of the PAM. DSBs are resolved by NHEJ or HR   | A well-established, conventional system; can be used to engineer a plethora of genetic modifications, ranging from nucleotide substitutions to chromosomal translocations; a single effector system which may be easier to use as opposed to multiprotein effector systems   | Off-target editing of genomic DNA may occur; uses a long sgRNA; uses a large endonuclease which may be difficult to package in viral delivery systems; introduces DNA DSBs which may have deleterious effects if not resolved properly, particularly for therapeutic applications  |
| CRISPR-Cpf1  | <i>Francisella novicida</i>   | Cpf1 pairs with a crRNA to introduce scattered DNA breaks at position 18 of the non-target strand and 23 of the target strand, leaving a 5' overhang. DSBs are resolved by NHEJ or HR  | Can be used to engineer a plethora of genetic modifications, ranging from nucleotide substitutions to chromosomal translocations; uses a different PAM than SpCas9, extending the range of possible target sites; a single effector system which may be easier to use as opposed to multiprotein effector systems; uses a short crRNA that may be easier to synthesize and deliver | Off-target editing of genomic DNA may occur; uses a large endonuclease (although smaller than SpCas9) which may be difficult to package in viral delivery systems; introduces DNA DSBs which may have deleterious effects if not resolved properly, particularly for therapeutic applications                                      |
| Cascade-Cas3 | <i>Thermobifida fusca</i>     | Cascade pairs with a crRNA to recruit Cas3, a highly processive DNA helicase-nuclease, which nicks the non-paired DNA strand and unidirectionally shreds the target DNA upstream of the PAM sequence in a 3' to 5' orientation                             | Can be used to generate large deletions; uses a short crRNA that may be easier to synthesize and deliver   | Off-target editing of genomic DNA may occur; large multiprotein effector which can be difficult to package for viral delivery; limited in the scope of editing; no control over the length of the deletions  |
| CRISPR-CAST  | <i>Scytonema hofmanni</i>     | Cas12k and Tn7-like transposase components pair with a sgRNA to insert large DNA cargo unidirectionally in a 5' LE to 3' RE orientation 60–66 nt downstream of the PAM. A 5 bp integration site is duplicated and found 5' and 3' of the cargo integration | Can be used to insert large DNA elements up to ~10Kb   | Off-target editing of genomic DNA may occur; insertion results in the integration of flanking sequences and duplication of the integration site; a multiprotein effector which can be difficult to package for viral delivery; uses a long sgRNA; limited in the scope of editing; demonstrated efficacy only in bacterial systems |

*doping*” could pose unprecedented challenges for anti-doping agencies and sports-governing bodies worldwide.

#### IV. Challenging Ethical Considerations – Diverging Wall of CRISPR

Figure 1. Table briefly summarising the mechanism, advantages and limitations of CRISPR

Despite its medical potential, the application of CRISPR technology raises several ethical dilemmas. Some of these remaining ethical concerns for the usage of CRISPR technology will be discussed in this section. Primarily, it can be deduced that since CRISPR intends to target specific genetic sites, there might occur plausible scenarios where it implants the planned changes ‘at sites other than intended ones’.<sup>17</sup> This is called “off-target” mutations, which are one of the unintended modifications that CRISPR technology can produce – due to CRISPR being ‘subjected to the bases within the ~20 nucleotide sequence of the sgRNA’.<sup>18</sup>

<sup>17</sup> *Supra* note 6 at p 21.

<sup>18</sup> Antara Barman et al., ‘A glance at genome editing with CRISPR-Cas9 technology’ (2020) *Current Genetics* 66(3), 447–462, p 452-3.

Consequently, this can potentially lead to many adverse and highly unwarranted effects.<sup>19</sup> Hence, the technology could in this way do more harm than good. This is the case, despite its advantage of being relatively precise and a discovery that ‘inactivation of Cas9 immediately after target site cleavage was found to reduce off-target sites effect’.<sup>20</sup> This is also the case despite a development being made with regards to *anti-CRISPR (Acr)* proteins which act as an “off-switch” for the technology that work as a means to control CRISPR activity.<sup>21</sup> Such adverse effects can only be predicted, but their implications may be daunting and irreversible which results in scepticism towards usage of the method. The table below shows a concise summary of the science behind such off-targeting – contrasting it with the advantages that CRISPR technology has to offer. The question remains whether humans are willing to take the risks over these projected improvements.

Additionally, the possibility of germline editing, which involves altering genes in human embryos, presents fundamental challenges by raising questions about the moral and legal concept of medical *consent* and the ethical implications of the existence of the so-called “designer babies”.<sup>22</sup> There is a certain complexity attached to this argument. Primarily, medical professionals are obliged to provide full information to the patients – including potential risks that can occur within the treatment. This is something that is inherently linked to the Hippocratic oath ‘Primum non nocere’.<sup>23</sup> However, it is rather challenging to disclose such risks within CRISPR technology as there are a variety of complications that can occur afterwards and disclosing all may be impossible.

Subsequently, the potential for misuse of CRISPR technology in creating genetically modified organisms and the discussions about its ethical vitality create a next of kin issue of whether and how it should be regulated. Thus, as a response to address these ethical issues, regulatory frameworks are being pursued. Their aim is ensuring that every application of CRISPR is meant to prioritise human health and safety over any commercial interest.<sup>24</sup> Undoubtedly, as CRISPR technology continues to constantly evolve, the need for robust regulatory frameworks becomes more pressing on a daily basis. Countries around the world have begun to establish guidelines on gene editing, but discrepancies in regulations can lead to disagreements and even broadening of ethical dilemmas.<sup>25</sup> Especially in terms of international research collaborations.<sup>26</sup> Noteworthy, in such arrangements, the consideration of tests on human subjects and law regulating *consent* to such trials are of significance – as they vary

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<sup>19</sup> Sumbul Saeed et al., ‘Genome Editing Technology: A New Frontier for the Treatment and Prevention of Cardiovascular Diseases’ (2023) *Current Problems in Cardiology* 48(7), p 13.

<sup>20</sup> *Supra* note 18 at p 452.

<sup>21</sup> *Supra* note 5 at p 12.

<sup>22</sup> Bartha Maria Knoppers and Erika Kleiderman, ‘“CRISPR babies”: What does this mean for science and Canada?’ (2019) *Canadian Medical Association Journal* 191(4), E91–E92.

<sup>23</sup> Helen Askitopoulou and Antonis N. Vgontzas, ‘The Relevance of the Hippocratic Oath to the Ethical and Moral Values of Contemporary Medicine. Part II: Interpretation of the Hippocratic Oath – Today’s Perspective’ (2018) *European Spinal Journal* 27:1491-1500.

<sup>24</sup> Kyle E. Watters et al., ‘The CRISPR revolution and its potential impact on global health security’ (2021) *Pathogens and global health*, 115(2), 80–92, pp 80-2, 85-6.

<sup>25</sup> Oligonucleotide Therapeutics Society, ‘Can There Be International Agreement on How to Navigate the Future of Genome Editing?’ (5 April 2023, <https://www.oligotherapeutics.org/can-there-be-international-agreement-on-how-to-navigate-the-future-of-genome-editing/>).

<sup>26</sup> Thorben Sprink, Ralf Wilhelm and Frank Hartung, ‘Genome editing around the globe: An update on policies and perceptions’ (2022) *Plant physiology*, 190(3), 1579–1587, p 1580.

between countries.<sup>27</sup> Maybe it would be the most efficient way to tailor a unified, single, international approach in this regard.<sup>28</sup>

As an illustration of the previous point – in the United States, the National Institutes of Health (NIH) has set forth guidelines for research involving human gene editing, emphasising safety and ethical considerations first.<sup>29</sup> Conversely, countries like China have reportedly adopted a more lenient approach, allowing for more rapid advancements but at the expense of stringent ethical scrutiny and tendency to undermine the notion of legal certainty for their citizens.<sup>30</sup> Another consideration would be if such unilateral agreement were to be concluded, would it be actually respected and binding? Especially, taking into account the fact that international law is rather difficult to enforce.

Another deliberation that is not purely ethical but an aspect that is worthy of mentioning, would be the public perception of CRISPR. As it is constantly influenced by media portrayal and scientific understanding, the picture of CRISPR technology is regularly being convoluted.<sup>31</sup> Most, if not all, of the articles written on the subject contain scientifically sound but at the same time overcomplicated wording. Hence, for those not having the relevant scientific or medical or any other related knowledge, such language is not familiar and, consequently, it is not understood. While many view CRISPR as a breakthrough technology with the potential to improve health outcomes – especially taking into consideration the awarded Nobel Prize in 2020 and its gained popularity as a result. Others express concerns about the consequences associated with gene editing and the possibility of exacerbating social and legal inequalities in access to such therapies.<sup>32</sup> This is something that could be connected to the previous point regarding the regulation of CRISPR Cas-9. Having regard to that, it is vital that proper education and public engagement are secured in order to foster informed discussions about CRISPR technology and the implications it already has. CRISPR Cas-9 brought about plenty of advantages, and it would be ignorant not to make use of those. Therefore, ethical considerations should be enhanced instead and integrated into public discourse – highlighting both the benefits and potential risks associated with its application, as done by Yuan-Chuan Chen in his work.<sup>33</sup>

## 1. CRISPR in Sports: The Doping Dilemma and Competitive Fairness

The intersection of CRISPR technology with competitive sports presents a unique array of ethical challenges that transcend conventional medical ethics and were already briefly touched

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<sup>27</sup> A stance observed based on the general principle of *informed consent* used in medical law (especially the law of medical malpractice/negligence).

<sup>28</sup> *Supra* note 25.

<sup>29</sup> ‘Chapter 2: Oversight of Human Genome Editing and Overarching Principles for Governance’ in National Academies Press (US), ‘Human Genome Editing: Science, Ethics, and Governance’ (Washington, 2017).

<sup>30</sup> Pallab Ghosh, ‘China’s new human gene-editing rules worry experts’ (6 March 2023), <https://www.bbc.com/news/science-environment-64857311>.

<sup>31</sup> See example: The Economist, ‘The safety of CRISPR-Cas9 gene editing is being debated’ (21 July 2018), [https://www.economist.com/science-and-technology/2018/07/21/the-safety-of-crispr-cas9-gene-editing-is-being-debated?utm\\_medium=cpc.adword.pd&utm\\_source=google&ppccampaignID=18151738051&ppcadID=&utm\\_campaign=a.22brand\\_pmax&utm\\_content=conversion.direct-response.anonymous&gclid=aw.ds&gad\\_source=1&gad\\_campaignid=18151761343&gbraid=0AAAAADBuq3IKeYaFgiRqMsvZ92xuV68T1&gclid=CjwKCAjw9anCBhAWEiwAqBJ-cxBLQzNhW-EBaGI4V1WEJf5uOA0IIJsbURCqjGxSXmHz70rH\\_GdZXBoCbYEQAyD\\_BwE](https://www.economist.com/science-and-technology/2018/07/21/the-safety-of-crispr-cas9-gene-editing-is-being-debated?utm_medium=cpc.adword.pd&utm_source=google&ppccampaignID=18151738051&ppcadID=&utm_campaign=a.22brand_pmax&utm_content=conversion.direct-response.anonymous&gclid=aw.ds&gad_source=1&gad_campaignid=18151761343&gbraid=0AAAAADBuq3IKeYaFgiRqMsvZ92xuV68T1&gclid=CjwKCAjw9anCBhAWEiwAqBJ-cxBLQzNhW-EBaGI4V1WEJf5uOA0IIJsbURCqjGxSXmHz70rH_GdZXBoCbYEQAyD_BwE); BBC News, ‘Gene-edited babies: Current techniques not safe, say experts’ (4 September 2020), <https://www.bbc.com/news/health-54014969>.

<sup>32</sup> *Supra* note 6.

<sup>33</sup> *Ibid* at p 23-5.



upon – encompassing considerations of fairness, the integrity of competition, and the fundamental definition of human athletic achievement. Based on the information that was gathered on the CRISPR therapy in this article, a couple of points can be made in this regard.

a) The therapeutic use vs the enhancement use

A primary ethical concern pertains to distinguishing between legitimate therapeutic interventions and performance enhancement. Where does treatment conclude, and enhancement commence? For a Paralympic athlete with a genetic muscular disorder, CRISPR therapy intended to restore *normal* muscle function could be regarded as medical treatment. Conversely, if the same technology were employed to augment muscle development beyond *typical* human capabilities, it would constitute genetic doping – a form of cheating that fundamentally compromises fair competition.

The World Anti-Doping Agency (WADA) has already recognised gene doping as a prohibited method, defining it as ‘*the non-therapeutic use of cells, genes, genetic elements, or modulation of gene expression, having the capacity to enhance performance*’.<sup>34</sup> Nevertheless, the detection of CRISPR-based modifications presents significant technical challenges, as edited genes become indistinguishable from naturally occurring genetic variations.

b) Accessibility and equity in sports

Even when employed therapeutically, CRISPR technology engenders concerns regarding equitable competition across various sports disciplines. Should CRISPR therapies become available for the treatment of genetic conditions affecting athletic performance, access to such interventions will likely be contingent upon financial resources, geographic location, and healthcare infrastructure. Elite athletes from affluent nations with advanced medical systems may gain access to gene therapies that are unavailable to competitors from developing countries, thus establishing an uneven competitive landscape that favours economic privilege over innate talent and dedication. Or even so, enhancing such an uneven competitive landscape, as those nations that will be able to implement CRISPR therapy usually already have those advantages with more financial resources, more facilities, etc.

However, such disparity would be particularly accentuated within Paralympic sports, where athletes from diverse nations encounter substantial inequalities in access to adaptive equipment, training facilities, and medical support, which is obviously more needed for athletes battling hard training alongside diseases or other medical issues. The introduction of CRISPR therapies in this context could intensify existing disparities, potentially giving rise to a *genetic divide* between athletes who can afford state-of-the-art gene editing treatments and those who cannot.

c) The nature of athletic achievement

One of the most philosophical inquiries presented by CRISPR technology in the realm of sports pertains to the very essence of athletic achievement. Sports historically and inherently honour human potential, dedication, rigorous training, and the natural variability in human capabilities. If athletes were to alter their genetic composition to enhance their performance, it would fundamentally question our existing understanding of competition and success attained through personal effort.

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<sup>34</sup> Leslie Pray, *Sports, gene doping, and WADA* (2008) Nature Education 1(1), 77.

Specifically, regarding Paralympic athletes, this issue introduces intricate considerations concerning disability, identity, and the fundamental purpose of adaptive sports. Many Paralympic athletes consider their disabilities to be an integral part of their identity and oppose the notion that they require *fixing* or *curing*.<sup>35</sup> They have already accepted the struggles they have lived with. The availability of CRISPR-based therapies could exert pressure on athletes with genetic conditions to pursue gene editing to maintain competitiveness, potentially undermining the Paralympic movement's celebration of human diversity and various forms of physical ability or even push athletes to make choices that are not necessarily and truly theirs.

#### d) Regulation and detection challenges

In contrast to conventional doping substances that are identifiable through blood or urine examinations, modifications to an athlete's genome using CRISPR technology would be exceedingly challenging to detect. Once genetic alterations are made, they function similarly to natural genetic sequences, rendering them virtually indistinguishable from inherited variations. Current methodologies for testing primarily focus on identifying foreign DNA delivery vectors or abnormal gene expression patterns.<sup>36</sup> However, as technological advancements continue, these markers may become undetectable.

Moreover, the existence of varying regulations regarding CRISPR across different countries presents opportunities for *genetic tourism* wherein athletes may travel to nations with more permissive regulatory frameworks to undergo gene editing procedures prior to returning to compete at the international level.<sup>37</sup> This regulatory disparity complicates the efforts to ensure fair competition across borders and highlights the necessity for international collaboration in developing unified standards for gene editing within sports contexts.

## V. Conclusion

In conclusion, this paper has traversed the multifaceted landscape of CRISPR-Cas9 technology – exploring its revolutionary potential in medicine alongside the ethical and moral quagmires it engenders. From its origins as a bacterial defence mechanism to its current status as a cutting-edge gene-editing tool, CRISPR has demonstrated remarkable versatility and precision. Its applications span a wide array of medical fields, including the treatment of genetic diseases, cancer immunotherapy, and regenerative medicine, offering innovative solutions that were once relegated to the realm of science fiction. It is a hope for both the patients and the medical professionals. A hope of beating the diseases that were once thought to be unbeaten.

Nonetheless, the emergence of CRISPR technology is accompanied by various challenges and complexities. The potential for *off-target mutations*, ethical considerations surrounding germline editing, and the intricacies of informed consent raise significant questions regarding the responsible application of this technology. Questions that remain to be answered. These issues become increasingly complex when considering the use of CRISPR in sports, where the boundary between therapeutic intervention and performance enhancement becomes markedly indistinct. The technology introduces unique challenges for Paralympic athletes and the wider

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<sup>35</sup> Anne Marcellini, *The extraordinary development of sport for people with dis/abilities* (2018) European Journal of Disability Research 12-2, 94-104.

<sup>36</sup> Wolfgang Jelkmann and Carsten Lundby, *Blood doping and its detection* (2011) American Society of Hematology 188(9), 2395-2404 and Filomena Mazzeo, *From gene doping to athlete biological passport* (2016) Sport Science 9(2).

<sup>37</sup> Vera Lucia Raposo, *A Room with a View (and with a Gene Therapy Drug): Gene Therapy Medicinal Products and Genetic Tourism in Europe* (2022) Eur J Health Law 29(3-5), 504-520.

sporting community – pertaining to competitive fairness, accessibility, detection of genetic doping, and the fundamental nature of athletic achievement. Discrepancies in regulatory frameworks across nations further exacerbate these concerns, creating opportunities for regulatory arbitrage that may compromise fair competition in international sports. The importance of international cooperation and harmonisation is emphasised in both medical and sporting domains.

For the sporting community specifically, CRISPR technology requires urgent dialogue among athletes, sports governing bodies, anti-doping agencies, and ethicists to establish clear guidelines that safeguard both athletes' health and the integrity of competition at the same time. Paralympic sports organisations face the additional challenge of balancing the potential therapeutic benefits of gene editing for athletes with genetic conditions against the risk of creating new forms of inequality and pressures to conform to genetic 'norms'. Additionally, it is questionable whether such 'norms' could even constitute any sort of referring point.

Ultimately, the question whether CRISPR represents a revolutionary advancement, or a potential ethical danger remains open for debate. Nevertheless, such discussion and political discourses must be encouraged and enhanced. While its therapeutic potential is undeniable, the risks associated with its misuse cannot be ignored. Hence, in the future, it is imperative that scientists, policymakers, and the public engage in open and informed discussions to ensure that CRISPR technology is used in a manner that prioritises human health and safety while at the same time respecting ethical boundaries. Only through careful consideration and proactive regulation can the full potential of CRISPR be harnessed while mitigating its inherent risks.

## VI. List of figures

1. *Figure 1. Table briefly summarising the mechanism, advantages and limitations of CRISPR* - Yuan-Chuan Chen, '*CRISPR technology : recent advances*' (IntechOpen, 2023), p 23.

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