

# 1. Crispr-Edited World's First Horse – Science & Technology

World's first gene-edited Polo horses spark debate in Argentina. An Argentine firm created the world's first CRISPR-edited horses by suppressing the myostatin gene to enhance muscle growth for polo. This has ignited a global debate over genetic engineering's role in sports, animal welfare, and fair competition.

## Context – CRISPR-Edited Horses in Argentina

**Pioneering Development** – Argentina has successfully produced the world's first horses edited using CRISPR technology, a development that is initiating a global debate on the role of genetic engineering in elite sports.

**Company Involved** – The project was led by Kheiron Biotech, an Argentine biotechnology firm.

**Creation Process** – The firm created five foals that are clones of a prize-winning horse named "Polo Puraeza."

**Genetic Modification** – Using CRISPR-Cas9 technology, scientists performed a targeted gene edit to suppress the expression of the myostatin (MSTN) gene. The goal of this edit is to enhance muscle mass and sprinting ability in the horses.

## Understanding Gene-Edited Horses

**Methodology** – These horses are created by using CRISPR-Cas9 technology to precisely edit their genome, enhancing specific traits like speed, stamina, muscle growth, and recovery capacity.

**Distinction from Cloning** – Gene editing is fundamentally different from cloning. While cloning produces an exact genetic copy of an organism, gene editing alters specific DNA sequences within the genome.

**Technological Progression** – This marks a significant shift from the earlier practice of cloning polo ponies, which became prominent in the 2010s, to a more advanced approach of direct genomic intervention.

**Competitive Debut** – The introduction of these gene-edited horses into competitive polo circuits is the primary catalyst for the current worldwide debates on ethics and fairness in sports.

## Gene Editing Technology Explained

**Core Concept** – Gene editing is a scientific technique that allows for the modification of an organism's DNA sequences. This can involve changing a single base, removing a segment, or inserting an entirely new gene.

**The Process** – It typically involves three main actions on the gene of interest – insertion, deletion, and modification.

## CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) Technology

**Function** – CRISPR is a highly efficient and powerful gene-editing tool that enables scientists to add, remove, or alter genetic material at precise, targeted locations in a DNA sequence.

### Key Components –

1. **Cas9 enzyme** – This acts as a pair of molecular "scissors" that can cut the two strands of DNA at a specific location.
2. **Guide RNA (gRNA)** – A small piece of pre-designed RNA that guides the Cas9 enzyme to the exact spot in the genome where the cut is to be made.

**How It Works** – The guide RNA (gRNA) finds and binds to the target DNA sequence. The Cas9 enzyme follows the gRNA and cuts the DNA at that location. The cell's natural repair mechanisms then fix the cut. This can happen in two ways –

1. **Non-homologous end joining** – This method can be used to disable or "knock out" a gene.
2. **Homology-directed repair** – This method can be used to insert new genes or make specific corrections.

### Applications –

1. **Medicine** – Used in gene therapy, cancer research, and treating hereditary diseases.
2. **Agriculture** – Employed to create crops that are resistant to pests or resilient to climate change.

3. **Animals** – Utilized to enhance desirable traits, such as increased muscle growth in livestock or improved performance in racehorses.

**Advantages** – It is known for its high precision, is relatively cost-effective, and is significantly faster than older gene-editing methods.

## Other Gene Editing Technologies

### 1. TALENs (Transcription Activator-Like Effector Nucleases)

**Mechanism** – This method uses DNA-binding proteins (TALEs) derived from *Xanthomonas* bacteria, which are fused with a FokI nuclease enzyme to precisely recognize and cleave target DNA.

**Applications** – Correcting genetic diseases and creating disease-resistant plants.

**Advantages & Limitations** – Offers higher precision than ZFNs but is more complex, labor-intensive, and expensive than CRISPR.

### 2. ZFNs (Zinc Finger Nucleases)

**Mechanism** – As one of the earliest gene editing tools (developed in the 1990s), ZFNs use artificial zinc finger proteins designed to recognize specific DNA sequences, which are then fused with a nuclease to cut the DNA.

**Applications** – It was famously used in early clinical trials for HIV resistance.

**Advantages & Limitations** – It pioneered the field of programmable gene editing but is difficult to design, less efficient, and carries a higher risk of off-target cuts compared to newer technologies.

#### Base Editing

1. **Mechanism** – Introduced in 2016, this is a refinement of CRISPR that does not cut both DNA strands. Instead, it uses specialized enzymes to directly convert one DNA base into another (e.g., changing a Cytosine 'C' to a Thymine 'T').
2. **Applications** – Ideal for correcting single-point mutations, which are the cause of approximately 60% of known human genetic diseases.
3. **Advantages & Limitations** – It is more precise and safer than standard CRISPR but is limited to single-base changes and cannot perform large edits.

#### Prime Editing

1. **Mechanism** – An advanced version of CRISPR introduced in 2019, it functions like a "genetic word processor." It combines a modified Cas9 enzyme (nickase) with a reverse transcriptase enzyme to search, replace, insert, or delete DNA sequences with high precision.
2. **Applications** – Has the potential to treat complex genetic disorders like Tay-Sachs disease and sickle cell anemia.
3. **Advantages & Limitations** – It is extremely versatile and safer than standard CRISPR but remains in the experimental stage and faces challenges related to its delivery into cells.

## Challenges and Concerns of Gene Editing in Horses

#### Ethical Issues –

1. **Animal Welfare** – Concerns are raised about the potential suffering of animals during experimentation and the unknown long-term health effects of genetic modifications.
2. **Philosophical Debates** – The practice ignites discussions around the concept of "naturalness" and the ethical implications of "playing God."

#### Fairness in Sports –

1. **Unfair Advantage** – Gene-edited animals may possess superior abilities that create an unfair competitive advantage in sports like polo and horse racing.
2. **Spirit of Competition** – This threatens the principle of a level playing field, which is fundamental to the integrity and spirit of sports.

#### Regulatory and Legal Gaps –

1. **Lack of Frameworks** – Most sports governing bodies and regulatory authorities currently lack clear rules or frameworks to address the participation of gene-edited animals.
2. **International Enforcement** – The absence of uniform international guidelines makes it difficult to create and enforce consistent regulations worldwide.

### **Biodiversity and Genetic Risks -**

1. **Reduced Genetic Diversity** - An over-reliance on a few engineered lineages could significantly reduce the genetic diversity within the horse population.
2. **Increased Vulnerability** - A less diverse gene pool could make the species more vulnerable to new diseases, environmental stressors like climate change, or the emergence of harmful mutations.

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