Hypothesis

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Hypothesis

CRISPR: Challenges and Quantum Perspectives

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Abstract: Summary: This essay examines CRISPR-Cas technology, highlighting its potential and limitations in gene editing. While CRISPR enables precise DNA modifications for treating genetic diseases, its in vivo application faces major hurdles: low editing efficiency, delivery challenges, and off-target effects. Homology-directed repair (HDR) is inefficient, delivery methods are complex, and unintended mutations pose risks. A quantum-like genetic computation hypothesis suggests that CRISPR functions within a non-linear, probabilistic framework, challenging conventional methodologies. Ethical concerns include safety, consent, and legal regulation. The essay argues for a new quantum-informed research approach, integrating holistic, non-invasive methods like holistic medicine and nutrition to balance genetic interventions with natural biological processes. **Importance:** CRISPR is a groundbreaking tool for editing DNA with potential to cure diseases and improve crops, but real-world applications face major hurdles. Challenges like unintended mutations, delivery issues, and unpredictable effects must be solved for safe human use. This work highlights these obstacles and introduces a quantum-inspired perspective, suggesting genetic processes are more interconnected than previously thought. By rethinking gene editing within a holistic, balanced framework, this research advocates for safer, natural approaches to maximize benefits while minimizing risks.

Keywords: computational biology; CRISPR-Cas; gene editing; genome modification; DNA repair; Cas9 enzyme; genetic engineering; homology-directed repair (HDR); non-homologous end joining (NHEJ); off-target effects; delivery challenges; viral vectors; nanoparticles; liposomes; electroporation; microinjection; immunogenicity; mutation risk; quantum-like computation; lateral gene transfer (LGT); horizontal gene transfer; genetic plasticity; phenotype vs. genotype; therapeutic applications; ethical concerns; biological toxicity; gene therapy; precision medicine; quantum biology; non-invasive treatments; holistic medicine; self-healing ability; cellular balance; information encoding; biochemical reactions; protein interactions; bacterial immunity; spacer acquisition; genetic pathways; molecular diagnostics; public decision-making

Introduction

Genetic engineering is a cutting-edge field that offers endless possibilities to improve the quality of life. These cutting-edge methods involve modifying the genetic composition of cells to create new or enhanced organisms. This is achieved by transferring genes within or between species using recombinant DNA techniques and artificial DNA synthesis. The result is the creation of a DNA construct that can be inserted into the host organism. Gene engineering aims to fix inherent defects, such as genetic diseases and can bring relief to millions of people worldwide. The field of gene editing is becoming more versatile, offering new possibilities for research and development with the cost of declining and technology advancing. In light of these advancements, the world is for the better. (Uddin et al., 2020)

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is revolutionizing the genetic research landscape and applications as a revolutionary gene-editing technology. It is typically used with the Cas (for CRISPR-Associated) proteins (such as Cas9) for precise genome editing.

CRISPR allows for correcting genomic mistakes and regulating gene expression in cells and organisms rapidly, efficiently, and affordably. It is widely used in numerous laboratories for quickly

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creating animal and cellular models, functional genomic screens, and real-time imaging of the cellular genome. (Redman et al., 2016)

Mechanism of CRISPR

In the process of CRISPR-Cas gene editing, scientists first identify the sequence of DNA that causes a health problem. Then, they create a specific guide RNA that recognizes the particular strings of DNA components in that sequence. The guide RNA is then attached to the DNA-cutting enzyme, Cas, and introduced to the target cells. The complex locates the target DNA sequence and cuts it. After that, scientists can modify, delete or insert new sequences to edit the genome. Essentially, CRISPR-Cas acts as a cut-and-paste tool for DNA editing. (Hille & Charpentier, 2016)

It is truly remarkable how Emmanuelle Charpentier and Jennifer Doudna of the University of California, Berkeley, were recently awarded the prestigious 2020 Nobel Prize in Chemistry for their groundbreaking discovery of CRISPR/Cas9 genetic scissors. (Cohen, 2020) The innovative research has demonstrated its potential to cure genetic illnesses in mice by fixing specific damaged DNA. Moreover, the possibility of modifying human embryos using this technology is being explored. It is exciting to note that gene therapy, treatment of infectious diseases such as HIV, and engineering autologous patient material to cure cancer and other disorders are all promising therapeutic applications of CRISPR/Cas9. (Hille & Charpentier, 2016)

Advances in CRISPER-Cas Research

In 2005, Daniel H Haft and colleagues revealed 41 new CRISPR-associated (CAS) gene families in addition to the four already known. They also stated that CRISPR systems belong to various classes with distinct repeat patterns, gene sets, and species ranges. These mobile genetic elements are beneficial and may be essential in driving prokaryotic evolution. However, in a dynamic balance, most of them come and go rapidly from their host genomes. (Haft et al., 2005)

Hypothesis of Genetic Quantum-like Computation

CRISPR systems are highly diverse and, adaptable. The repeats exhibit significant structural and functional variability. The study identifies that major CRISPR subtypes are intricately associated with different patterns of Cas proteins. Dynamic evolutionary behaviour is represented by CRISPR loci. The subtypes are commonly passed from one species to another by lateral gene transfer (LGT) rather than by evolutionary lineages. Through horizontal gene transfer, CRISPR/Cas loci can spread between species and are not permanent. Reverse transcriptase domains are present in some but not all Cas1 proteins, suggesting that the processes behind the many CRISPR/Cas subtypes vary. Stability, gain, and loss of CRISPR loci are dynamically balanced during gene evolution. There are degraded CRISPR loci with incomplete or no Cas genes, indicating that stability, gain, and loss are dynamically balanced during gene evolution. (Silas et al., 2017)

Given the complexity of these interactions—where CRISPR elements exhibit non-linear evolutionary changes, probabilistic spacer acquisition, and modular recombination—it is reasonable to consider that the gene system functions within a quantum-like framework of biological genetic computation.

Current Situation of CRISPER-Cas in the Applications

More than 4000 different monogenic mutations cause at least 80% of all rare monogenic disorders. However, since we are aware of at least 6000 monogenic phenotypes, it is evident that this is not a comprehensive list of all the uncommon monogenic disorders. (Condò, 2022)

The theory of CRISPR-Cas gene-editing system is remarkable for simplicity, but it very likely leads to off-target effects and biological toxicity. Target specificity is a critical issue requiring improvement. In vivo editing efficiency is also lower than in vitro, making it unreliable for editing primary cells, specific tissues, and patients' bodies. Despite the challenges, many clinical trials use CRISPR-Cas to edit patients' cells in vitro. When the results go back to real human body environment,

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limited therapeutic efficacy and the lack of stability are found, awaiting further testing and improvement. (Liu et al., 2021)

Compared to non-homologous end joining (NHEJ), homology-directed repair (HDR) is a crucial aspect of CRISPR editing because it enables precise genetic modifications using a homologous template. However, HDR is significantly less efficient in most cells, as it occurs in a specific cell cycle, while NHEJ is active throughout. The accurate HDR is less efficient in vivo, which limits CRISPR's reliability, posing a major challenge for therapeutic applications. This limitation is critical for advancing CRISPR-based precision medicine. (Yang et al., 2020)

CRISPR editing faces critical challenges during the transition from Vitro to Vivo, a crucial shift from theoretical research to practical application on the human body. The challenges raise fundamental questions about the applicability of modern research methodology. In this context, the three major obstacles in technology editing efficiency, delivery, and off-targets come into sharp focus. (Liu et al., 2021)

As to the delivery, CRISPR editing may work efficiently in viral vector packaging, but not safe enough to correct gene defects and reach a new healthy balance. Physical delivery methods, such as electroporation and microinjection (Atluri et al., 2015), are often inefficient in vivo applications because the therapy of CRISPR editing has to deal with large numbers of cells efficiently, targeting specific tissues in a complicated cell environment, and fails to avoid damage to cellular balance caused by invasiveness. Non-viral vectors (nanoparticles, liposomes, exosomes) require complex designs to reach acceptable delivery. (Kim et al., 2024)

Because of the complexity of the structure and repeat sequence of CRISPR/CAS, unexpected DNA modifications are highly likely to introduce off-target effects. The human body may mount immune responses against bacterial Cas proteins. These challenges indicate that more than a single editing may be needed for the complex biological environment of living bodies. CRISPR-Cas tools are being used to correct genetic variants to cure these diseases, but the knowns and the parts that can be manipulated are limited. At the same time, the unknowns are unlimited in quantum-like genetic calculation in the human body applications. (Uddin et al., 2020)

Discussion in Ethics Setting

Another essay discusses the ethical setting of CRISPR/CAS editing in similar domains to the challenges in the previous essay in three dimensions: risk/benefit, consent-related concerns, and legal concerns. The first risk/benefit mainly concerns safety. This is because gene modification is a critical decision that may not be easily reversible and even lead to a dynamic imbalance in the bottom layer of biological cell systems. The other two types of consent and legal-related concerns highlight the requirements to improve research methodology and applications. (Lange & Kappel, 2022) All of these have brought up the fundamental discussion, which is increasingly moving towards a discussion of a new research methodology which can resolve quantum biological genetic computing.

CRISPR Discussion in Quantum Setting

The simplicity of gene editing technology is an inherent weakness in the quantum biological setting, not only in the scope of quantum technology in the research but also radically in the methodology of research from the quantum perspective. CRISPR faces challenges and risks in quantum biology, such as mutation, immunogenicity, and genotype vs. phenotype. Quantum biology analyses the real biological environment through quantum calculation. It is essential to understand the fundamental quantum interactions that determine the properties of biological systems at the structure of the cell level. (Ewaisha & Anderson, 2023)

Many biological processes convert energy into a form that can be used for chemical transformations. These processes are potentially quantum mechanical and involve chemicals, light energy, reciprocal micro magnetic field and electric field, and electron and proton transfer in chemical processes such as photosynthesis, olfaction, and cellular respiration. Scientists use computational models to simulate the interactions of microscopic components of organisms by reducing biological processes to fundamental physical and biochemical reactions. However, it is difficult to accurately

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study the microscopic essence of these reactions under the current scientific situation, resulting in uncertainty in the macroscopic results. Currently, four main life processes have been identified that are affected by quantum effects: enzymatic catalysis, sensory processes, energy transfer, and information encoding. (Brookes, 2017)

Phages can evade the CRISPR-Cas immune system by randomly mutating their protospacer regions or PAM sequences. Point mutations dramatically lower the effectiveness of evading immunity in bacterial populations with substantial spacer diversity. This might be the case because the variety of spacers puts more adaptation pressure on the virus, which causes the invader to be eliminated quickly. (Yang et al., 2021) Apart from this, the cell might not always mend the break as intended, and we might accidentally break DNA at random locations in the genome, introducing fresh mutations that might impair the activity of other genes and have various adverse effects based on which gene or genes are impacted. (Mengstie et al., 2024)

The complexity of in vivo application might be far beyond what we can currently observe, which is reflected in the biological reaction with a single variant that appears as a "pathway." Recent studies have shown that Mu-like phages infect Pseudomonas aeruginosa and actively inhibit their host's CRISPR-Cas systems by producing anti-CRISPR (Acr) proteins. These proteins interact with components of the type I-F CRISPR-Cas interference mechanism. For example, AcrF1 and AcrF2 bind different subunits of Cascade, preventing the Csy complex from binding to the target DNA. AcrF3 was found to bind the nuclease Cas3, inhibiting its function in target degradation. Similar proteins have been shown to prevent type I-E CRISPR-Cas immunity in the same organism. (Hille & Charpentier, 2016) These series of reactions may completely counteract the control effect of CRISPR-Cas, which means that there may be many other unknown factors and reactions in the known pathway which lead to immunogenicity.

Analogous to quantum states, genes are discrete rather than continuous, and he genotype-phenotype distinction is drawn. The "Genotype" is an organism's complete hereditary information, while the "Phenotype" is its actual observed properties, such as morphology, development, or behaviour. This distinction is fundamental in the study of trait inheritance and evolution. The phenotype results from quantum calculation of internal and external factors, and it is the most natural and practical phenomenon. It is impossible to fully observe in labs. (Santiago-Alarcon et al., 2020)

Another risk of gene editing comes from the foundation of genetic research: A gene alone can neither cause an observable phenotypic trait nor be necessary and sufficient for the emergence of observable characteristics. A dynamic cellular environment, the computation of multiple additional genes, and particular physio-chemical conditions are required for gene engineering to have safe and practical effects on humans. (Orgogozo et al. 2015).

Conclusion

To Improve in Quantum Research Methodology

In a comprehensive analysis, especially when dealing with complex genetic problems, we observe that gene system is a complex quantum balance environment with the help of rapid development of modern quantum observation methods. Therefore, there is ample space for re-exploration in the methodology of the transformation process from traditional research to clinical application.

New means of quantum medical observation may include non-invasive, non-drug, and reversible natural methods such as traditional Chinese medicine, lifestyle regulations, comprehensive nutritional formulas, and psychotherapy. Use scientific measurement and statistical methods to evaluate and compare objective overall health indicators before and after entering the above treatment pathways that can coordinate the balance of the body's biological environment and make enhancing immunity and self-healing ability the primary goal to ensure that the treatment methods promote overall health are sufficiently safe and effective.

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