Recent Applications and Usages of CRISPR-Cas9 Gene Editing Technology

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Introduction

In nature, CRISPR, or Clustered Regularly Interspaced Short Palindromic Repeats, is a molecular mechanism that bacteria possess to defend against viral invaders through cutting the genome sequence of said invaders. When investigating bacterial defense mechanisms in 2012, biologists Dr. Jennifer Doudna and Dr. Emmanuel Charpentier found out that the cuts that the mechanisms make are highly specific and tied to specific genome sequences, subsequently harnessing its ability to edit genes synthetically. Their discoveries were thrust into the scientific spotlight, and ever since, scientists have found various ways to genetically engineer their own synthetic CRISPR mechanisms, which are able to make precise cuts in various cells and organisms.

Genetic editing is a huge topic of debate in the scientific community, but its contribution in advancing biosciences cannot be denied. CRISPR-Cas9 is an influential technique in the biotechnology sphere, and this article will explore the various recent applications and concerns about this gene editing tool in research, the clinic and beyond.

Perfecting Research with Genomic Editing

The precision of CRISPR-Cas9 gene cleaving opens doors for researchers to study genetic sequences in more depth and specificity. One example of such is using CRISPR in genome-wide screens, large-scale experiments that sequence large chunks of an organism's genome. With CRISPR, researchers can much more quickly identify mutations in large genomic sequences, saving time and perform more comprehensive analyses of common mutation patterns for other researchers to target for therapeutic interventions (Barrangou and Doudna, 2016). An increase in effectiveness of identification methods subsequently allow for more material for other researchers to work with in terms of practical applications of identified genetic issues.

Another example in which CRISPR has been used to further research efforts is the identifying of risk genes in neurodevelopmental disorders. Some psychiatric disorders such as schizophrenia and bipolar disorder are known to have genetic components. While large-scale genetic studies have been done to prove that these disorders have ties to genetic factors, finding and confirming these particular risk genes in a more effective way has been an issue. Using CRISPR, however, researchers can more efficiently transfer genes into more cost-effective, single-celled models. THE CRISPR-Cas9 mechanism would first cut off a segment of desired gene, and researchers would place that piece of genome into cell lines that are easier to study. In addition, CRISPR can also make small changes simultaneously in these cellular models, allowing for more effective and accurate identification of risk regions that lead to these major neurodevelopmental disorders (Kurishev et al., 2022).

These applications of CRISPR-Cas9 are largely restricted to researchers and the academic community. However, the attention of the CRISPR-Cas9 technology is garnering attention even from the general public, and that is through the medical applications of these discoveries.

Medical Therapeutics and "Treating" the Untreatable

While genetic research is important, it is largely confined to the academic community. The aspect of CRISPR applications that draws attention beyond the scientific community is its ability to change certain details in the human genome, potentially alleviating sufferers of certain disorders previously deemed untreatable.

CRISPR-Cas9 systems have been used to combat microbial infections. When the mechanism recognizes a disease-carrying entity within the body, it can cleave the DNA of the pathogen and subsequently eliminate bacterial populations in a body. While there are native systems that exist to do so, synthetic CRISPR-Cas9 systems have also been engineered by

different groups of researchers (Barrangou and Doudna, 2016). Combined with native systems, just about any bacterial sequence can be targeted and destroyed using CRISPR-Cas9, effectively removing harmful microorganisms in the body.

In addition, certain simple genetic disorders have been shown to be treatable through CRISPR-Cas9 technology. Sickle-cell anemia is an inherited blood disorder that is caused by errors in a singular gene. The mutated red blood cell is rigid and has a sickle-like shape, which leads to a hindered ability to carry nutrients to the body and will subsequently break down. It is often considered the most severe form of anemia and can be chronic. Because the HBB gene is only one main gene that leads to sickle cell anemia, correcting errors in the HBB genomic sequence using CRISPR-Cas9 can effectively "treat" sickle cell anemia, alleviating patients from the chronic condition (Bhattacharjee et al., 2022).

For diseases with no exact cure but have genetic risk factors, CRISPR can still reduce the probability of getting a certain disorder. For example, Alzheimer's disease is generally considered to have no current cure. A general risk gene associated with Alzheimer's is ApoE4 and is expressed by most brain cells. In a study, CRISPR has been used to inactivate the ApoE4 risk gene within a mouse model, leading to healthy mice no longer predisposed to Alzheimer's disease (Bhattacharjee et al., 2022). Similar experiments have also been conducted with other genetically predisposed disorders such as cardiovascular diseases.

Beyond the Clinic and the Lab

The genome editing technology of CRISPR-Cas9 has profound uses in medical research and applications, but that does not mean its usage is only constricted to those fields. For example, a team of researchers led by Andrew Hammond found that CRISPR could be used to edit out malaria-transmitting genes in female mosquitoes and reducing their fertility, but not to

the point that the mosquito population is no longer able to survive (Hammond et al., 2016). Experiments like these provide a possible alternative to solving public health issues stemming from organisms and similar bugs, but without the harm of destroying the ecosystem that values the contribution of such organisms.

CRISPR has also been applied outside of healthcare. Researchers have found that CRISPR could be used to create new starter cultures, which form the basis for many common dairy-fermented foods such as yogurts and cheeses (Barrangou and Doudna, 2016). Food scientists could use CRISPR to not only generate new flavors of fermented foods in a consistent way, but also artificially protect the bacteria from being infected by common agents of foodborne illness. Another set of researchers also used CRISPR to increase the expression of genes that form the basis of nutrients such as Vitamin A and zinc in crops (Kumar et al., 2022). These crops would have more nutrients per unit weight compared to current commercially available vegetables. Kumar and his team believe that these genetically-fortified crops could pave the way for alleviating issues of food security and world hunger due to not being particularly expensive to produce long-term.

Gene editing is powerful. CRISPR is applicable in various disciplines, but it does come with its risks and ethical dilemmas that slow down its research and development.

Ethical Considerations

When Dr. He Jiankui, a Chinese researcher, revealed that he modified the genes of two human embryos so they would not carry AIDS, much of the scientific community expressed outward disapproval at his actions, so much that he had to remove his academic affiliations due to intense social pressure. The technology of CRISPR gene editing is slowly becoming more and more mature, but at the same time, the scientific community is also becoming more and more

wary of what it means to change the flow of natural evolution. While most applications of CRISPR as of now focus on the genes of an individual, there has been some effort in editing germline cells, which can affect the posterity of the genetically engineered individual far into the future. Dr. Jennifer Doudna, one of the pioneers of CRISPR gene-editing technology, has called for a worldwide halt of pushing CRISPR research until the scientific community can come to a near-consensus of what it means to have the power to edit genes, and how far the technology should be allowed to go.

CRISPR-Cas9 is an influential bioengineering tool that has the potential to change livelihoods, but as Dr. Doudna states, until there is a more concrete understanding about the ethical ramifications of gene editing, there needs to be mindfulness of how this technology is used and applied in society.

References

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