**[The Future of Genomic Editing]**

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The purpose of this microreview is to examine the process of genomic editing and its successors, specifically Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR). Briefly speaking, CRISPR made its corrections to the genome through breaking the strand of DNA to make repairs using the specific endonuclease, Cas9. This process of gene repair using CRISPR and Cas9 is thought to be extremely rapid despite its significant attention to small details. Mutations on the gene tend to be negatively linked to cancer and multiple other human genetic diseases. This major advancement in the molecular life sciences field has proven successful in working to solve this issue through multiple experiments and research, which is fueled towards progressing potential solutions. There is evidence of its success and acceptance in the science world through its recent received awards, specifically being named as *Science’s* Breakthrough of the Year. Through continuing general knowledge of this type of genomic editing, significant improvements are observed in those suffering from genetic disorders for future years to come.

**Introduction**

With the rise of the world of genomics specifically in the past forty years, most positive advancements are welcome to the world of molecular life genetics to assist in solving our disease-filled world. However, many of these gene-editing tools were not discovered purposely. Genetic editing is defined as a permanent alteration to the organism’s DNA through mutations. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) is an example of a genetic repair mechanism that was discovered solely as a fortunate accident (Ishino, 2018). Originally discovered in an Escherichia coli organism decades ago, the correlation between CRISPR and Cas9 was not established until the early 2000s. Further information regarding CRISPR was discovered when it was first recognized in Archaea in the late 1990’s. The Archaea discovery presented many contributions to the progression of scientific knowledge in this subject. This is due to the greater complexity of Archaea in comparison to Escherichia coli. However, correlation between CRISPR and Cas9 was created in the early 2000’s following increased research when comparing multiple genomes. This interaction created the CRISPR-Cas9 system from the two previously known components of gene editing.

Previously speaking, genetic mutations to an organism’s DNA have been thought to be harmful, however CRISPR-Cas9 uses mutations to its advantage (Humphreys, 2016). This adaptive immune response introduces breaks to the double stranded DNA through use of the protein and endonuclease Cas9. Following the break of the double stranded helix, CRISPR will be introduced to manipulate the strand and implement the needed mutation. This CRISPR molecule is presented as RNA, and therefore, it is easily recognizable by the strand.

**Recent Progress**

An issue regarding the original CRISPR-Cas9 editing system was the inaccuracy of targeting double stranded breaks and mutations (Humphreys, 2016). Although serving effective to its intended targets, additional mutations were also occurring due to lack of specificity by the response. Some advancement was made to work towards improving this issue with the system. This includes increased use of single guide RNA (sgRNA) that assists in the specificity of Cas9 and in the neutralization of charges in the system to ensure that only target mutations are being made. This second improvement is known as SpCas9 and is thought to be more reliable in ensuring the specificity of CRISPR-Cas9 in its mutations. When working towards solving human genetic disorders, it is important that the correct mutations are being introduced as additional ones could serve as more of a problem than solution.

Additionally, recent research has demonstrated the effectiveness, timeliness and affordability of this genetic editing tool versus more established ways of introducing mutations to the body (Humphreys, 2016). The ease and minimal cost of CRISPR gene editing in comparison to other genetic editing methods is quite drastic. Therefore, the amount of times that gene editing can be repeated to ensure accuracy in the mutation versus through other methods is substantial. Some of these other methods may possess longevity in terms of scientific lifespan. These include Zinc Finger Nucleases (ZFNs) and Transcription Activator-like Effector Nucleases (TALEs). However, ZFNs and TALEs present many disadvantages to their use in effective gene editing. These adverse circumstances include cost, effective labor, time, and inability of some nucleases to bind or activate. In comparison to the thousands of dollars that will be invested in effective ZFN and TALE, CRISPR is a minimal thirty dollars to successfully mutate the genome.

The most recent progress of the three is the patent war over the claiming of CRISR-Cas9 gene editing in eukaryotic organisms (Buhr, 2017). The debate resonated from the lack of clarification in who owned the patent in non-eukaryotic and eukaryotic organisms. This patent war was debated heatedly between University of California Berkeley versus the Broad Institute of MIT and Harvard. The case was ruled in the favor of Broad Institute of MIT and Harvard to hold the rights of CRISPR-Cas9 in genomic editing of eukaryotic organisms. The patent war contributes to the recent progress of CRISPR-Cas9 by solving the issue at hand so that advancements in gene editing may continue to occur. It is to be expected that further developments will be discovered as the complexity of organism dealt with continues.

**Discussion**

CRISPR-Cas9 gene editing brings a whole new technology to the world of genomics (Humphreys, 2016). These mutation techniques are thought to be capable of improving human genetic disorders through altering the double stranded DNA. One specific disease that CRISPR gene therapy is thought to potentially cure is sickle cell anemia which alters the ability of hemoglobin to carry oxygen throughout the body by a mutation. Additionally, other diseases that could eventually be successfully cured through this process are Duchenne muscular dystrophy and kidney disease. Although developments in working to cure these diseases have been made, they have not progressed to the point of developing a specific cure through the mutations of CRISPR. However, genetic cures are on the horizon through continuations of the recent progress as depicted above. With continued expansion and development of the CRISPR technology as well as fixation of specificity issues, cures are expected in the near future.

Counteracting the viewpoints that CRISPR is in the near future for solving genetic diseases served recent research conducted in 2015 (Mo, 2015). Throughout this research, embryos that were considered unable to produce life were tested using CRISPR techniques to examine their success rates. This research addressed the need to examine results impacting children affected by CRISPR and the severe detail that must be present in the specific mutations. Although much research has been conducted and tests ran regarding CRISPR, there is still more progress and money to be spent towards perfecting this technique. Money and time, things of significant value in the science world, must still be readily available to aid in creating an appropriate gene editing technique for eukaryotic organisms out of this technology.

Although the obvious positive effects associated with CRISPR are evident and proven, there are some additional factors that could negatively impact the influence held by *Science’s* Breakthrough of the Year. Critics are quick to examine the ethical value on both sides of the spectrum whether CRISPR advancements should be withheld until perfected by the science community or if these advancements will serve of greater risk and concern than benefit. Considerations of ethics and how future generations will be affected by the genetic mutations must always be examined before furthering the expansion of this seemingly promising technology.

**References**

Buhr, S. “The CRISPR patent battle is back on as UC Berkely files on appeal.” *Tech Crunch*. (2017).

Humphreys, B. “Gene Editing: Powerful New Tools for Nephrology Research and Therapy.” *Journal of the American Society of Nephrology,* (2016) 28:1350-1361. Doi:10.1681/ASN.2016020146.

Ishino, Y., Krupovic, M., & Forterre, P. “History of CRISPR-Cas from encounter with a mysterious repeated sequence to genome editing technology.” *Journal of Bacteriology*. (2018). Doi:10.1128/JB.00580-17.

Mo, O. “CRISPR-Cas9 Human Genome Editing: Challenges, Ethical Concerns and Implications.” *Journal of Clinical Research & Bioethics, (2015):* 6:253. Doi: 10.4172/2155-9627.1000253.