The Implications of SCD and CRISPR Cas-9

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Many people around the world suffer from a variety of genetic disorders, one in particular being Sickle Cell disease. The people who suffer from this genetic disorder face different levels of severity and symptoms, suffering from anemia and pain (due to the distorted shape of their blood cells), and the disease can be inherited through different mechanisms (Rees et al.). Currently, its symptoms can be alleviated through the use of Over-The-Counter pain relievers and blood transfusions. Without a doubt, our future depends on our ability to utilize and implement effective treatments and therapies to reduce and diminish the existence of genetic disorders, including Sickle Cell disease. Most notably, gene therapy for the treatment of genetic diseases/disorders has the potential to serve as an excellent tool to treat diseases that currently have no treatment or cure, all encoded by our highly cryptic, highly specialized DNA. If we delve into our research and developments, we could have the possibility to manipulate genetic variability, as well as create facilitated life circumstances and new discoveries that correspond with the human genome (Sharma et al.). This paper will investigate the use of CRISPR technology to treat Sickle Cell diseases, diving into the specifics of the disease and the mechanism, as well as the complications and controversy that arise.

Sickle cell disease (SCD), is caused by a mutation in the hemoglobin protein, and inhibits red blood cells from effectively delivering oxygen to other parts of the body, resulting in fatigue and weakness throughout the day (Elendu et al.). Hemoglobin is a highly specific protein — with multiple subunits of amino acids/peptide chains — and sickle cell disease occurs when a mutation in the HBB gene is present, converting the glutamic amino acid into valine, which alters the protein's primary structure (Elendu et al.). Consequently, the round shape of the red blood cells morphs into a rigid & sickle shape, and blockages are prevalent as oxygen is unable to undergo transportation through these cells. Fortunately, early detection of Sickle Cell disease can help patients manage the disease and its risks efficiently: techniques include screening tests such as peripheral blood smears, hemoglobin separation techniques, and genetic tests (Arishi et al.). To continue, sickle cell disease is inherited in an autosomal recessive pattern, making it susceptible only to people who are unfortunate enough to inherit the gene from both of their parents. Remarkably, Sickle Cell disease — known to be a hazardous genetic disorder — has advantages when it comes to Malaria, where it is most prevalent in the tropical and subtropical regions of Africa (Elendu et al.). Carriers of the Sickle Cell disease (in other words, those who only carry one recessive allele, and not the two that are required to inherit the disorder) benefit from reduced risk of extreme Malaria symptoms as the Malaria parasite is less likely to survive in sickle-shaped blood cells (Naik and Haywood). Sickle Cell heterogeneity is significantly protective when it comes to Malaria, as Sickle Cell homogeneity brings its own risks relating to blood cells, while people without the inherited gene(s) are more prone to severe Malaria symptoms (Naik and Haywood). Though Sickle Cell disease can be dangerous, there are a variety of non-profit organizations and support groups working to alleviate pain and provide healthcare.

Given the severity and scale of this genetic disease, treatment options to improve the lives of those suffering from Sickle Cell is critical. Although much is still not known about SCD, researchers and scientists are developing new gene editing tools with the purpose of modifying/altering DNA, to cure these diseases and replace the mutated genes with the unmutated ones. Currently, the most common gene editing technology is CRISPR Cas-9, a tool that holds limitless possibilities and discoveries for the future, as well as a multitude of controversies (Sharma et al. 9). Possessing a great value of therapeutic potential, CRISPR Cas-9, also known as “Clustered regularly interspaced short palindromic repeats”, is simple, efficient, and highly precise — qualities which are essential for treating a specific part of the genome (Sharma et al. 9). The CRISPR Cas-9 system consists of the protein, Cas-9, which can cut the double strands of DNA at a precise location, so that only one specific area is changed (Ma et al.). The guide RNA, consisting of merely 20 bases, comes along with a long scaffold piece, and the RNA binds to the DNA with the assistance of PAM, which allows Cas-9 to effectively recognize and interact with its DNA site. In the case of Sickle Cell Disease, CRISPR Cas-9 must target the HBB gene mutation. After making a specific cut in the DNA, the Cas-9 protein allows DNA polymerase (an enzyme that adds complementary nucleotides) to replace the faulty nucleotides. These reparations may include insertions, deletions, or substitutions at a target site (Zhang et al.). DNA ligase, an enzyme that seals up the repaired DNA, ensures that the nucleotides in the DNA strands are joint and continuous. To illustrate, if a person who has lived with Sickle Cell their entire life visits a specialized treatment center, then medical specialists can use CRISPR-Cas9 to edit their stem cells, activating a fetal hemoglobin gene. After the process is complete, the modified stem cells are permeated back into their bloodstream, similar to a blood transfusion.

Furthermore, clinical trials assess the efficiency and accuracy of medical treatments, which not only enhance healthcare for certain individuals, but for society in its entirety (Umscheid et al.). Clinical trials must follow a set of ethical principles, using a complex methodology as well as the foundations of trial design and oversight, and approval from a therapeutic (Umscheid et al.). Through the implementation of clinical trials, healthcare providers are able to determine which medical therapies are the most effective, allowing for pharmaceutical industries to sell accurate treatments to help patients (Umscheid et al.). Additionally, clinical trials are used for CRISPR Cas-9, and the methodology of CRISPR Cas-9 allows for disease-carrying individuals to get rid of their diseases in a simple and safe way; however, in addition to the numerous advancements CRISPR brings to gene therapies, it remains a topic of controversy in the field of gene editing for scientists, researchers, and the public (Jc and G). Consequently, people have gained awareness of the fact that designer babies and embryos can be modified to fit their own desires and expectations, instead of CRISPR’s main purpose of disease treatment. During the 5th congress on controversies in preconception, preimplantation, and Prenatal Genetic Diagnosis, in collaboration with the Ovarian Club Meeting, a variety of professors with bioethical and medical backgrounds convened to discuss whether gene editing is ethical, and they decided it is not safe for it to be used in human embryos for clinical purposes (Jc and G). This decision utilized significant evidence and reasoning, enhancing its validity, because the negative repercussions of CRISPR Cas-9 could affirm stereotypes, increase susceptibility to societal pressures, etc. Thus, clinical trials have played a significantly large role in ensuring that CRISPR Cas-9 is effective, efficient, and safe to implement as a treatment mechanism (Umscheid et al.). While there are a multitude of ethical

questions regarding the use of CRISPR, unlike other gene editing mechanisms, CRISPR Cas-9 aims to target the source of the problem instead of simply alleviating symptoms. Even so, undoubtedly, CRISPR Cas-9 is an important tool for extrapolating potential cures and treatments.

In essence, genetic disorders can pose a major challenge to the lifestyles and quality of life of many affected individuals; hence, scientists and researchers in the gene editing field are in the process of inventing and testing possible therapies, a significant one being CRISPR Cas-9. This gene editing mechanism serves as a simple and specific way to target the faulty nucleotides and repair the DNA, reversing the negative effects of a certain genetic disorder. In the case of Sickle Cell Disease, a genetic disorder that alters the shape of red blood cells, CRISPR Cas-9 can replace the faulty HBB nucleotide. Clinical trials are essential to ensuring that CRISPR Cas-9 is capable of repairing DNA successfully, without any flaws or errors in the process. Ultimately, genetic disorders, repair mechanisms, and clinical trials all act together as a dynamic system, allowing us to expand and advance our knowledge of gene editing and therapies.

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