Using CRISPR to Cure Sickle Cell Anemia Can Alter Its Chemical Structure

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Introduction

Sickle cell anemia is a rare blood disorder that is generally passed down from genetics. Sickle cell anemia a severe type of anemia that have additional difficult features compared to various other types of anemias. The erythrocytes, like in all anemic disorders, are misshapen and are unable to carry oxygen throughout the body. The cause of its irregular shape and inability to carry oxygen is due to the hemoglobin that is encoded in the genes. The hemoglobin protein plays a significant role in carrying oxygen due to being composed of a heme iron group.

Luckily in addition to one of CRISPR's inventions was the creation of Casgevy and Lyfgenia. These two are a type of gene therapy that specifically cures Sickle Cell Anemia by simply altering the genes that code for the mutation and produces one of the highest oxygen hemoglobin carrier, HbF, Fetal Hemoglobin. It has been found that as CRISPR is modifying the DNA, it is changing the chemistry in the human body. Overall, I will research on exactly how big of a change that chemical change is and if it impacts the body.

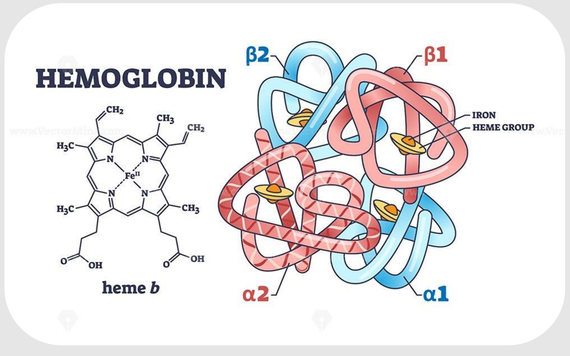

Figure 1: An image showcasing the chemical structure of a heme group within the hemoglobin.

Materials/Methods

The entire purpose of this research is to discover if CRISPR alters the iron absorption levels within the body when altering the genes to encode for HbF. Although I do not have any access to CRISPR or gene editing tools, I was able to gain a blood sample of a recipient who is anemic. The purpose of this is to view the cell of someone who is anemic or has sickle cell anemia and compare it to a normal erythrocyte. This way we can all visualize how the mutation that causes Sickle cell anemia can change the structure of the cell. In addition to that, I will further my research by researching on primary sources regarding CRISPR, Casgevy, and Lyfgenia.

Experiment - Wright stain
Equipment:
brightfield microscope
Drop of blood sample
sterile lancet
3.8g of Wright stain powder
100ml methanol
Pure drinking water

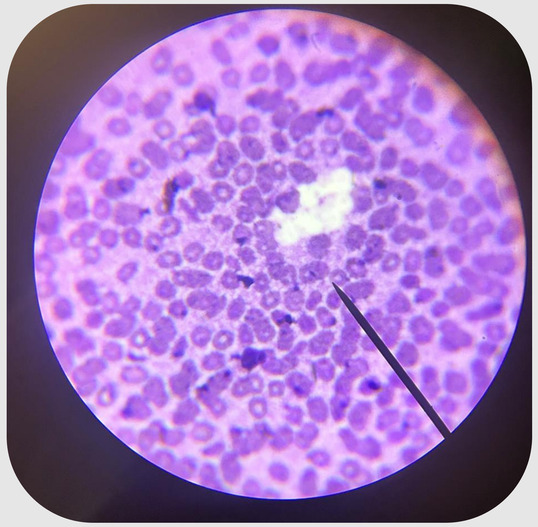

Figure 2: An image showcasing the erythrocytes from the Wright-Giemsa stain

Results

Wright-Giemsa Stain Results

- Misshapen erythrocytes
- Blood Platelets
- Leukocytes
- Granules

No Glycerol and buffer solution included!

There seems to have been many misshapen red blood cells from the recipient and blood platelets.

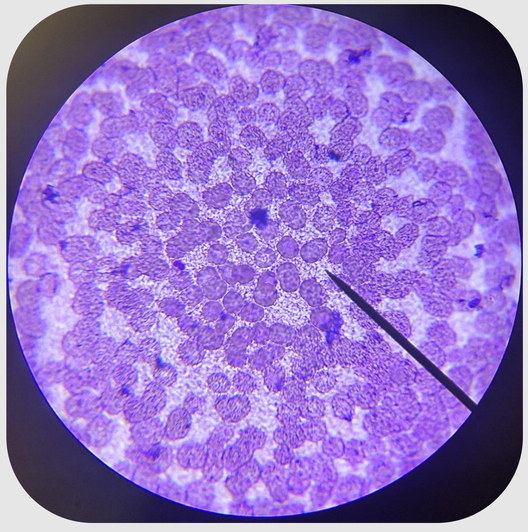

Figure 3: An image showcasing the erythrocytes from the Wright-giemsa stain.

Discussion/ Conclusion

Hemoglobin is a protein within erythrocytes that has the ability to transport Oxygen throughout the body. It consists of four globin subunits in which each contain a chain that is connected with non-protein heme group. Due to its chemical structure, it has the ability to bind to a heme group. There are three hemoglobin types of A, A2, and F in which each are then synthesized in different codes.

Gene-editing Tools for SCD
Casgevy, aka Exagamglogene autotemcel, modifies blood stem cells and transplants them back into the bone marrow, allowing them to multiply and promote the production off HbF. Lyfgenia uses lentiviral vector and modifies the gene to produce HbA T87Q-globin for patients who have other blood disorders not associated with SCD. The same process goes by transplanting it back into the bone marrow after modification and allow replication.

Since gene editing tools are able to change a specific targeted area of a gene to encode a specific protein to be read, that protein is basically being synthesized. Therefore, if the recipient with anemia wanted to change the genetic code that is producing the mutation for their sickling nature in their RBCs by one of the two tools, they would be changing their overall chemical structure of their heme group. Not to mention since HbF has a higher affinity to oxygen compared to HbA, their iron absorption levels in the body are higher which is due to their subunits being alpha and gamma subunits in addition to their heme group.

Their overall chemical structure of the hemoglobin has changed with a gene editing tool, but their chemical structure of the heme group has not changed. Nevertheless, it is still a tetramer polymer protein that have 4 subunits and a Fe(II) in the middle of the Porphyrin ring that combines to the oxygen.

References

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