Investigating Driver Mutations in Sickle Cell Treatments

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Research in Context

Sickle Cell Disease (SCD) is a genetic condition which affects the red blood cells in your body. This condition causes the shape of your red blood cells to change. This can cause painful blockages in blood vessels for an individual.

A cure for Sickle Cell Disease is to genetically alter a person's Stem Cells so that they are able to make healthy red blood cells again.

As the dangers of this treatment are unclear, this poster aims to identify some of the most common mutations in a person's genes which could cause further complications later in life (mainly cancers) to people who have been treated in this way

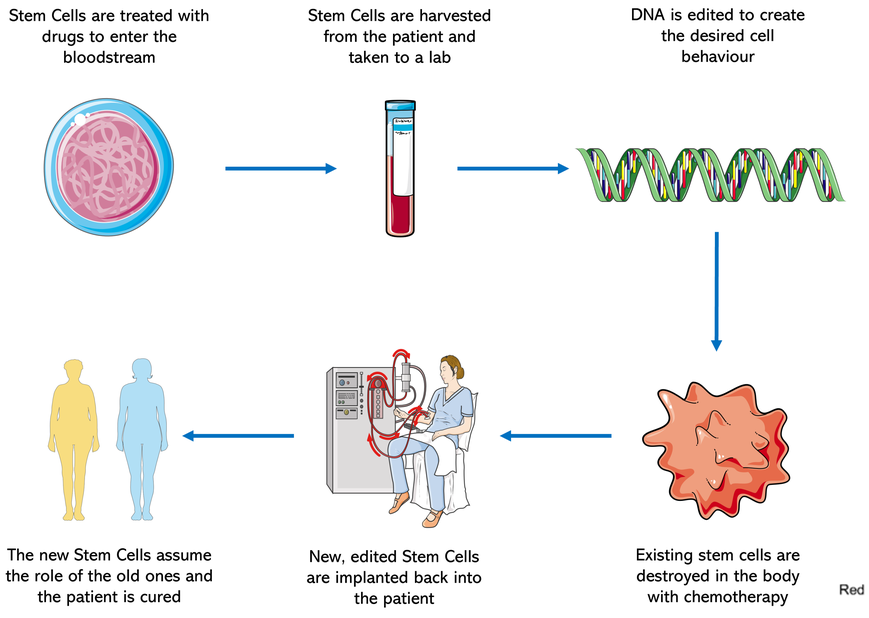

Figure 1—A flowchart showing the process by which cells are gene edited to cure a patient of Sickle Cell Disease.

Our Findings

Seven driver mutations were identified in the preliminary work achieved by this lab.
This review paper was responsible for finding more information about four key contenders.

1 **TP53**
Responsible for stopping tumour formation in healthy cells.

2 **CDKN2a**
A "checkpoint moderator" to help regulate the cell cycle

3 **DNMT3a**
Important for the cessation of protein production in cells.

4 **PPM1d**
Chief gene regulator of the "cell under stress" response.

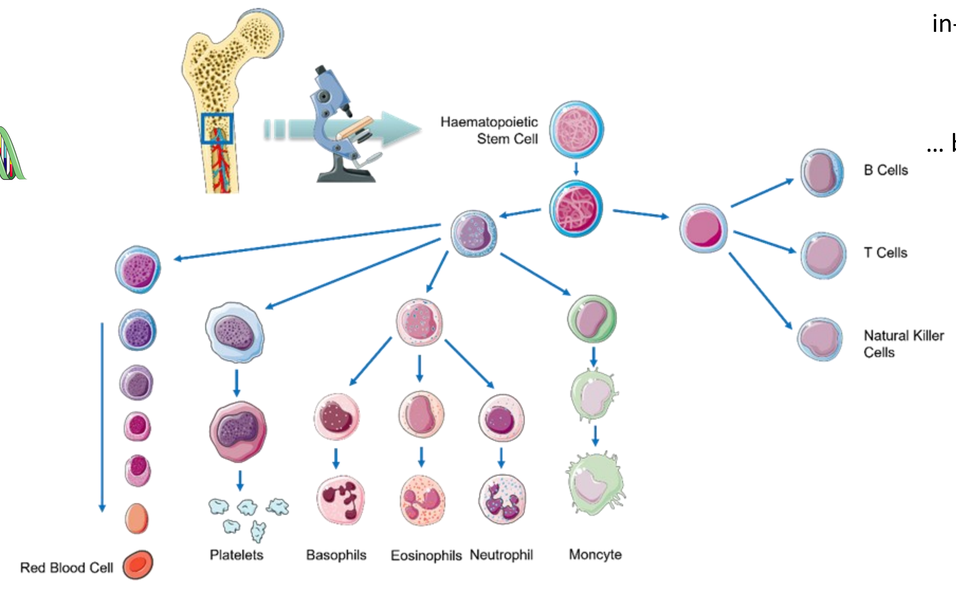

Figure 2—A diagram showing the most basic pathway of haematopoiesis. All blood cells originate from stem cells, and go through a series of cell divisions and differentiate into different subtypes of blood cell. The most common are red, and white blood cells. Sickle Cell Disease affects the red blood cells.

Moving Forward

The four mutations detailed above prove significant short- and long-term risk to patients, leaving them susceptible to many chronic illnesses of the blood.

We need to...

... conduct **experiments** in a **larger cohort** of patients in order to get a better understanding of how common these mutations are in people who have been treated for Sickle Cell Disease.

... aim to identify the **root cause** of the mutations—during which step of the process do the mutations in transplanted cells arise?

... study the mutations over a **long period of time**, both in-vivo and in-vitro to understand how likely these mutations are to develop into cancers in these patients.

... begin looking at ways to potentially **mitigate future risk** for this incredibly effective life saving treatment based on the most current, up to date research on the topic.

References

1. Parts of the figure were drawn by using pictures from Servier Medical Art. Servier Medical Art by Servier is licensed under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/).
2. *Sickle cell disease - NHS*. (n.d). Accessed September 19, 2022, from https://www.nhs.uk/conditions/sickle-cell-disease/
3. Chapman, M. S., Cull, A. H., et al (2022). *Clonal dynamics after gene therapy in sickle cell disease*. *manuscript in revision*.

Interested to learn more?
Find out more about Sickle Cell Disease here.
Information taken from the nhs.uk website

Interested to find more about the research?
Find out more about the research here.
Contact information can be found by scanning the code.