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Investigating potential Driver Mutations found in patients undergoing Gene Therapy for Sickle Cell Disease

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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 shape and, instead of being a disc shape, they appear to be crescent shaped. Because of this change in shape, the blood cells can be too large to fit through blood vessels and can cause immense pain to the individual, known as sickle cell crisis. People with SCD are also at a higher risk of developing conditions such as strokes and heart attacks. SCD is a relatively common genetic disease, affecting about 15,000 people in the UK. Since its genetic linkage was discovered around 70 years ago, there haven't been many major advances in the treatment of SCD.

The most potent curative treatment at present is a bone marrow transplant, in which hematopoietic stem cells (cells which are responsible for the creation of red blood cells), HSCs, are transplanted into a patient to increase the number of healthy red blood cells produced. This treatment in many ways should be flawless, however finding a matching donor can be tricky. Through advances in gene technologies, we can alter stem cells from the patient to make them healthy instead of using a donor, although there are significant health and safety concerns in doing this.

The lab I am involved with have just received funding by the Bill and Melina Gates foundation to explore this disease more, so my project will be centred around this disease in the form of a research question "investigating potential driver mutations found in the stem cells of patients undergoing gene therapy for sickle cell disease". This topic is tremendously fascinating to me, as it is on the forefront on curative measures in patient models. This will be great experience for me to fuel my desire to learn, as I am interested in research and haematology, and it will give me a strong basis for which to progress in my career.

This project will link into two of the research themes expressed by the University. Under the theme of new technologies, I will use this as a chance to get familiar with the cutting-edge technology used to sequence genetic information and how to analyse it to identify potential mutations. Under the guise of the 'health and wellbeing' theme, I will look at real patient data and assess which of the mutations identified may be potential causes of other diseases, and I will look to analyse the frequency of these mutations within a cohort. With these research themes in mind, I propose that I will create a guide for anyone who may want to analyse this data in the future, along with some guidance on the most common mutations which have potential to cause diseases. I will also look at categorising the frequency of some of these mutations and aim to look at the 'serial-offenders' and offer up ways to research their effect in more detail.