Structural analysis of retinoic acid receptor-related orphan receptor gamma in complex with FM26

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INTRODUCTION

Sickle cell anemia or sickle cell disease is a genetic disease of red blood cells. Normally,RBC's are disc shaped which give flexibility to travel through small blood vessels, with this disease the rbc's have an abnormal crescent shaped resembling a sickle. This makes them sticky and rigid and prone to get trapped in small vessels which blocks from reaching different parts of body, causes pain and tissue damage.SCD is an autosmal recessive condition. We need two copis of the gene to have the disease. If we have only one copy of the gene, we are said to have sickle cell trait. This has symptoms such as excessive fatigue, fussiness in babies, swelling and pain in hands and feet, frequent infections, pain in chest, arms, back and legs. Hemoglobin is the protein in red blood cells that carries oxygen. It normally has two alpha chains and two beta chains. The four main types of sickle cell anemia are caused by different mutations in these genes.

Hemoglobin SS disease is the most common type of sickle cell disease. It occurs when you inherit copies of the hemoglobin S gene from both parents. This forms hemoglobin known as Hb SS. As the most severe form of SCD, individuals with this form also experience the worst symptoms at a high temperature.

Hemoglobin SC disease is the second most common type of sickle cell disease. It occurs when you inherit the Hb C gene from one parent and the Hb S gene from the other. Individuals with Hb SC have similar symptoms to individuals with Hb SS. However, the anemia is less severe.Hemoglobin SB+ (beta) thalassemia affects beta globin gene production. The size of the red blood cell is reduced because less beta protein is made. If inherited with the Hb S gene, you will have hemoglobin S beta thalassemia. Symptoms are not as severe. Hemoglobin SB 0 (Beta-zero) thalassemia is the fourth type of sickle cell disease. It also involves the beta globin gene. It has similar symptoms to Hb SS anemia. However, sometimes the symptoms of beta zero thalassemia are more severe. It is associated with a poorer prognosis.People who only inherit a mutated gene (hemoglobin S) from one parent are said to have sickle cell trait. They may have no symptoms or reduced symptoms.

Blood tests : Several blood tests can be used to look for SCD, Blood counts can reveal an abnormal Hb level in the range of 6 to 8 grams per deciliter.,Blood films may show RBCs that appear as irregularly contracted cells.Sickle solubility tests look for the presence of Hb S.HB electrophoresis- Hb electrophoresis is always needed to confirm the diagnosis of sickle cell disease. Imeasures the different types of hemoglobin in the blood.

A number of different treatments are available for SCD: Rehydration with intravenous fluids helps red blood cells return to a normal state. The red blood cells are more likely to deform and assume the sickle shape if we are dehydrated .Treating underlying or associated infections is an important part of managing the crisis, as the stress of an infection can result in a sickle cell crisis. An infection may also result as a complication of a crisis.Blood transfusions improve transport of oxygen and nutrients as needed.

HYPOTHESIS

A fraction of erythrocytes appear as target cells in stained blood smears in sickle cell disease, due to a inheritance of the hemoglobin variant Hb S, polymerizing upon deoxygenation. These cells appear in a three dimension as thin cups. A process of their formation in this disease is proposed based on a band 3-based mechanism of the erythrocyte shape control, able to explain the erythrocyte echinocytosis by glucose depletion. It indicates that their formation is due to a stomatocytogenic slow outward transport of the dibasic form of endogenous Pi with an H(+) by band 3, promoted by the decrease of the Donnan ratio, which decreases cell pH and volume, attributed by a decrease of cell KCl concentration by the higher efflux of K(+)Cl(-) cotransport and Ca(2+) activation of the Gardos channel. Its implications are briefly discussed with respect to target cells per se, target cell formation in other hemoglobinopathies, acquired and inherited disorders of the lipid metabolism and dehydrated hereditary stomatocytosis as well as a stomatocyte presence in a double heterozygote of Hb S and Hb C and of an involvement of the process of target cell formation in acanthocytosis in acquired and inherited disorders.

EXPERIMENTAL DESIGN

In order to understand the overall organization of the sickle cell anemia i.e analysis of retinoic acid receptor related orphan receptor gamma in complex with FM 26 (PDBID – 6T4G) . The analysis includes the evaluation of the secondary structure followed by hydrogen bonding using the PYMOL SOWFTWARE . The X-RAY DIFFRACTION method is used here .

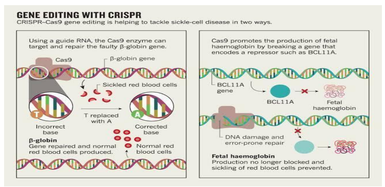

FIGURE 1 – GENE THERAPY : Erasing sickle cell anemia using crispr. Katherine Bourzac

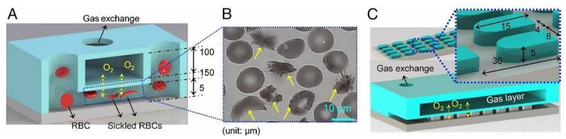

FIGURE 1 - **Kinetics of sickle cell biorheology and implications for painful vasoocclusive crisis.**

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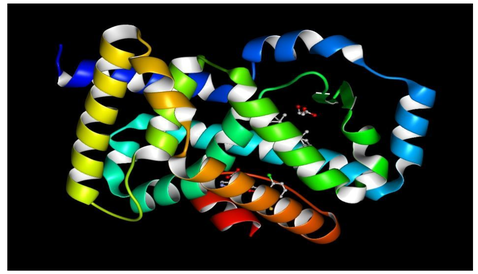
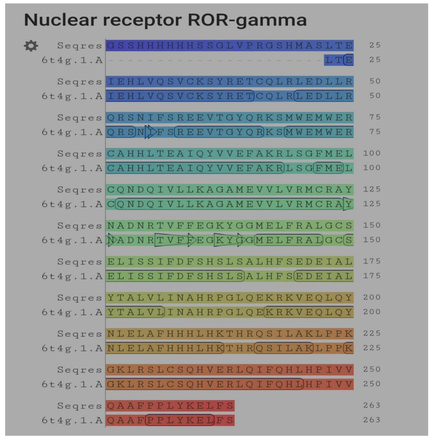


GURE 2 – PYMOL STRUCTURAL VIEW



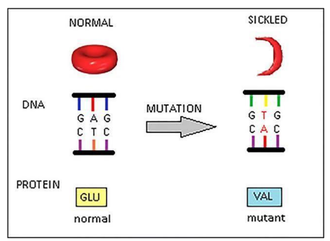
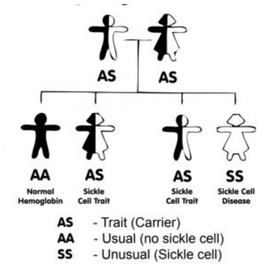


FIGURE - 4 Non-invasive urinary biomarkers of renal function in sickle cell disease



RESULTS & DISCUSSION

The structure of sickle cell anemia contains 10 alfa helix and 3 beta strands in it It has no hydrogen bonds in it . Followed by the structural analysis a nuclear gamma receptor is activated in the site of mutataion . This molecular modeling was also done earlier.

Sickle cell anemia is curable with crispr editing and by other techniques and technology.

REFERENCES

Medically reviewed by Graham Rogers, M.D. — Written by the Healthline Editorial Team — Updated on June 10, 2019

https://en.m.wikipedia.org/wiki/Sickle_cell_dis

Canessa M. Hematol Oncol Clin North Am. 1991. PMID: 1650770 Review.

e-poster presented online at the ABFR-2020.