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Analysis of Three variants of HBB and Their Association with Sickle Cell Anemia

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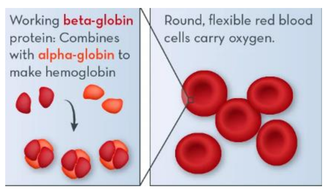
ABSTRACT

Sickle cell anemia is a disease that is caused by the mutated HBB gene. This disease is inherited from two parents who have this mutation trait. Another disease that HBB gene is associated with is beta-zero thalassemia. Beta-zero thalassemia is caused by a lack of beta chain. This means less hemoglobin is made which results in too few red blood cells. The purpose of this study is to show how different variants of the HBB gene can affect sickle cell anemia. Simple ClinVar was used to determine the presence of the HBB gene in sickle cell anemia. Poly-Phen2 and SIFT showed how amino acid substitution can predict the effect of a missense mutation. Swiss modeling was used to show protein homology. HBB stands for hemoglobin subunit beta. This gene is only found in humans. The superfamily of the HBB gene is globin-like. The globin-like conserved domain is used as an oxygen transporter and intracellular signaling pathways. The HBB gene has 417 missense mutations. The missense mutations Glu7Lys, His3Arg, and Trp38Ser were analyzed. The HBB gene is found to be expressed in bone marrow and the placenta. This is significant because some sickle cell anemia patients require bone marrow transplants for treatment. According to SIFT, the mutation Glu7Lys is predicted to be tolerated with a score of 0.07. For Poly-Phen2, the score for Glu7Lys is likely to be benign with a score of 0.005. The SIFT prediction for His3Arg is predicted to affect the protein function with a score of 0.03. For Poly-Phen2, the score for His3Arg is predicted to be benign with a score of 0.003. According to SIFT, the mutation Trp38Ser is predicted to affect protein function with a score of 0.00. For Poly-Phen2, the score for Trp38Ser is predicted to probably be damaging with a score of 1.000.

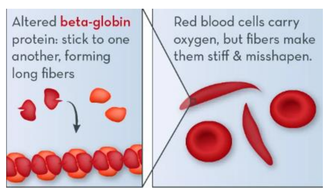
INTRODUCTION

Sickle cell anemia has only one gene which is HBB. HBB is also known as ECYT6, CD113t-C, and beta globin. The structure of the two different types of polypeptide chains in adult hemoglobin, Hb A, is determined by the alpha (HBA) and beta (HBB) loci. The two alpha and two beta chains make up the typical adult hemoglobin tetramer. Instead of appearing as a normal circular shape, their blood cells are sickled. Unfortunately, there is no cure for sickle cell anemia. Some symptoms of sickle cell anemia include shorter life span, painful episodes, vision problems, and frequent infections. This project aims to demonstrate the potential effects of various HBB gene mutations on sickle cell anemia.

Normal Erythrocyte



Sickled Erythrocyte

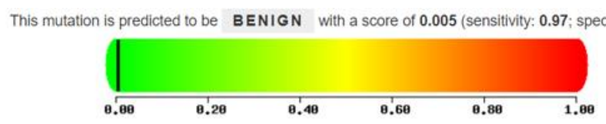


METHODS

- Simple ClinVar was used to determine the presence of the HBB gene in sickle cell anemia.
- SIFT was used to predict whether an amino acid substitution would affect the protein function.
- Poly-Phen2 showed how amino acid substitution can predict the effect of a missense mutation.
- Swiss modeling was used to show a 3-D model of the HBB gene.

RESULTS

SIFT and POLY-Phen2



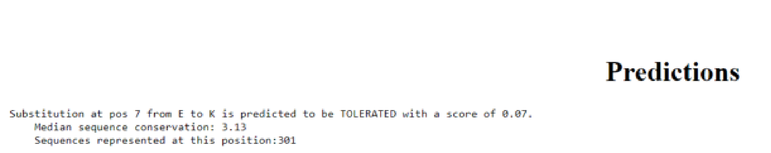
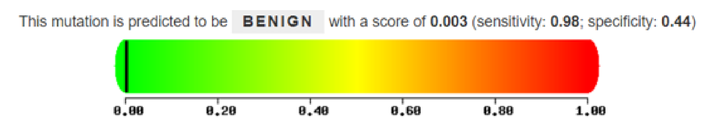


Figure 1 and 2: SIFT and Poly-Phen2 of Gly7Lys



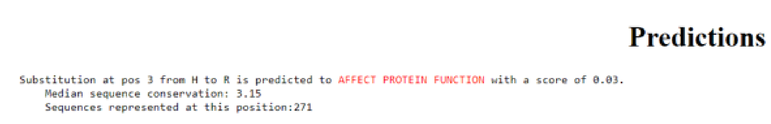
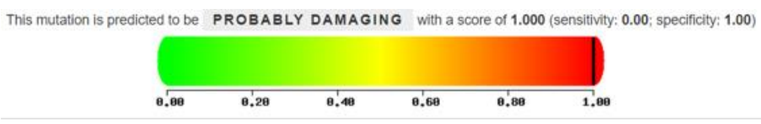


Figure 3 and 4: SIFT and Poly-Phen2 of His3Arg



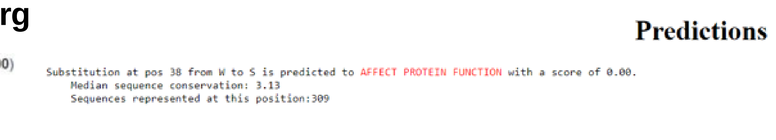
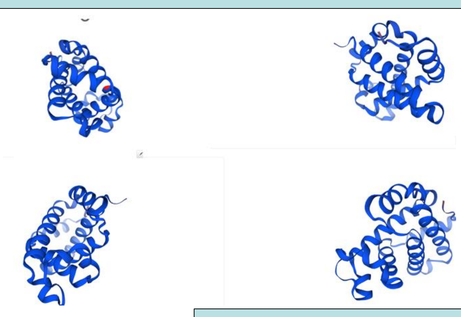
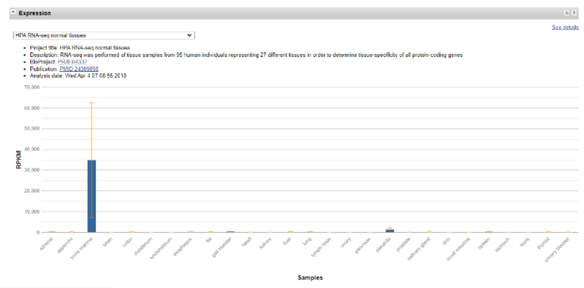


Figure 5 and 6: SIFT and Poly-Phen2 of Trp38Ser

SWISS Model

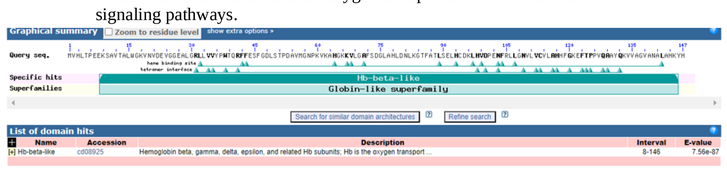


Expressivity of Gene



Conserved Domain

The superfamily of the HBB gene is globin-like. The globin-like conserved domain is used as an oxygen transporter and intracellular signaling pathways.



DISCUSSION AND CONCLUSION

When a new amino acid is substituted, this can cause sickle cell anemia to develop. A missense mutation that was pathogenic was Glu7Lys. In total there were 46 pathogenic mutations for HBB. According to SIFT, His3Arg and Trp38Ser were both likely to affect protein function. According to PolyPhen-2, Trp38Ser is expected to probably be damaging with a score of 1.00. This means that these mutations contribute to the lack of oxygen in hemoglobin.

Another disease that the HBB gene is affected is oxygen transporting disorder. People with this disease have bluish skin because their blood tissue delivers less oxygen in the body. This research can help the medical community learn the background behind different forms of anemia. Even though this is no cure for sickle cell anemia, more research can be used to find more efficient treatment plans for this disease.

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