Genetic Markers Associated with Anemia in Individuals with Sickle Cell Disease in Tanzania

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Presentation outline

- Resume
- Research Interests
- Introduction
- Methodology
- Results and Discussion
- Conclusion and Future work
- Acknowledgments

RESUME

- Dr. Liberata Alexander Mwita works as a Lecturer in the department of Pharmaceutical Microbiology at Muhimbili University of Health and Allied Sciences in Tanzania (MUHAS).

- She has a PhD in Bioinformatics from University of Pretoria, South Africa (2017).

- Her M. Sc in Biotechnology (2012) and B. Sc. in Molecular Biology and Biotechnology (2009) are both from University of Dar-es-salaam, Tanzania.

Research interest

1. Genome Wide Association Studies and Next Generation Sequencing analysis of Sickle Cell Disease in order to improve sickle cell disease management through understanding genetic mechanisms underlying the disease.

2. Microbiology, molecular biology, biotechnology and bioinformatics aspects of diseases.

INTRODUCTION

- Sickle cell disease (SCD) is a genetic disease caused by mutation in the hemoglobin (HBB) gene.

- The mutation causes shortage of healthy red blood cells (RBC) due to the polymerization of the RBCs into a sickle shaped red blood cells, these have a short life (10-20 days)unlike normal RBCs which live for 120 days.

Normal Red Blood Cell

Sickle Cell

Image from: https://kidshealth.org/en/teens/sickle-cell-anemia.html

INTRODUCTION

- Individuals with SCD experience anemia which increases the morbidity and mortality.

- The cure for SCD are stem cell or bone marrow transplant, they are very expensive hence can be afforded by very few individuals with SCD.

- Therefore SCD is managed through prophylaxis and treatment of complications related to SCD.

INTRODUCTION

- Despite the similarity in the origin of the disease, individuals demonstrate varying symptoms and severity.

- This research aims to identify genetic variants associated with anemia in individuals with SCD.

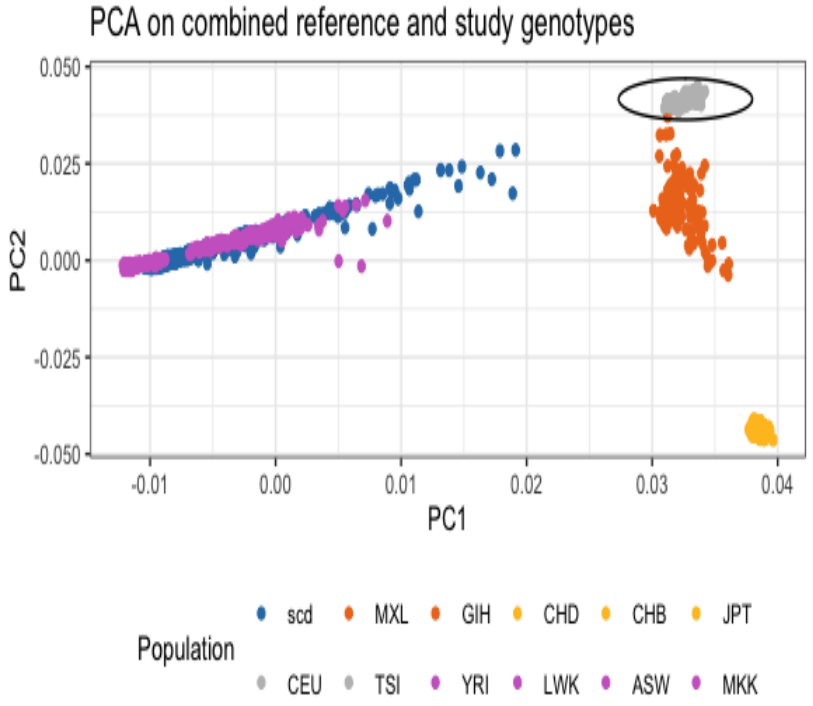
- The quick identification of single nucleotide polymorphisms (SNPs) related to anemia in SCD will enable better prediction of the severity of anemia that the individual will experience which will facilitate better preventive treatment.

Methodology

- Samples were collected, DNA extracted and genotyped, details are described in Mtatiro et al., 2014.
- Quality control of the genotype data was performed using PLINK software.
- Association of the phenotype (Hemoglobin) to the genotype was performed using PLINK software.
- Genotype imputation and replication study design is in progress.

Results and discussion

Fig. 1 shows the relationship of the quality controlled genotype data from our study to other populations.



Key:
In blue: scd is our study population

In purple: YRI (Yoruba, Nigeria), LWK (Luhya, Kenya),ASW (Africa ancestry in Southwest USA), MKK (Maasai, Kenya)

In grey: CEU (Utah, North and West European), TSI (Toscan, Italia)

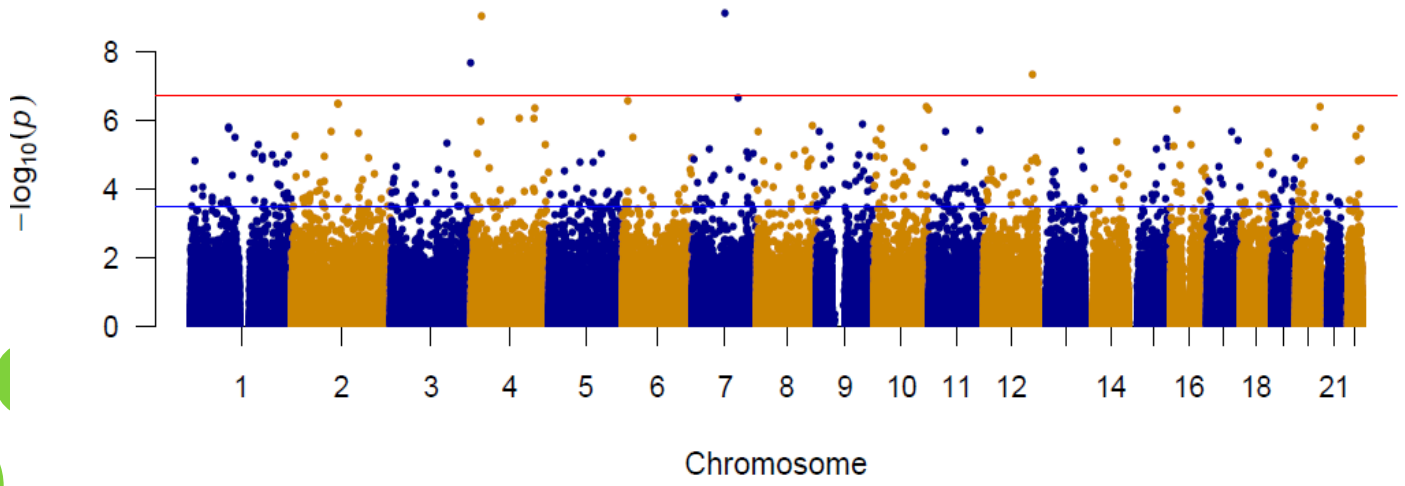
In yellow: CHD (Chinese, Metroplolian Colorado) CHB (Han Chinese, China), JPT (Japanese, Tokyo)

In orange: MXL (Mexican, California), GIH (Gujarati Indians, Houston-Texas)

Our study population (blue dots) is admixture, most of individuals cluster with individuals of African ancestry while few individuals deviate from the cluster. The individuals deviating from the cluster are of Arabic and Indian origin.

Results and discussion

Fig. 2 shows the SNPs (red and blue dots), the p-values are on the y-axis and the chromosome in which the SNPs belong is on the x-axis.



The Manhattan plot shows the most significant SNPs (above the red line) that associate with anemia in SCD are located in Chromosome 3, 7 and 12.

Results and discussion

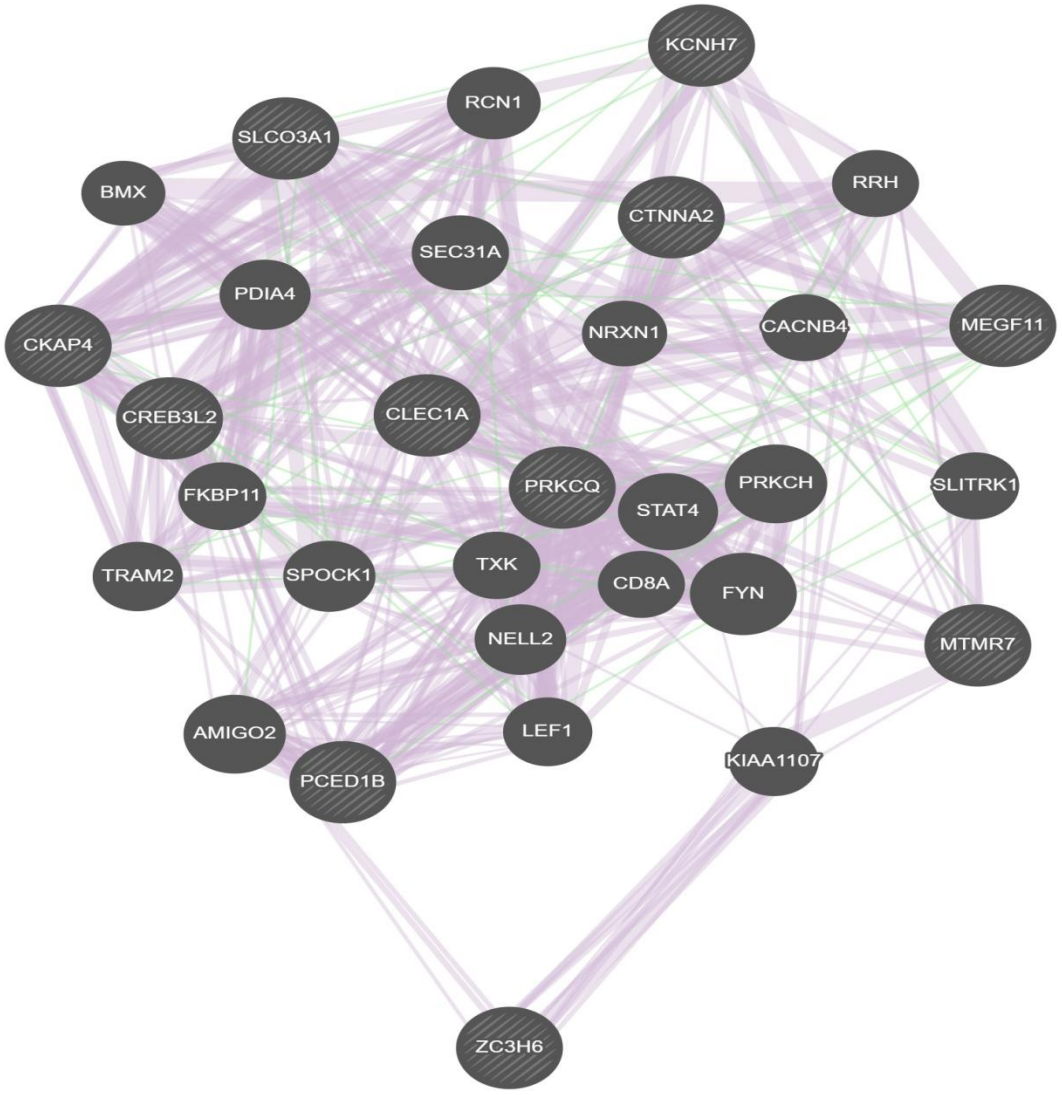
Table 1: Some of the SNPs that associate with anemia in individuals with SCD, the chromosome and the genes in which they are located.

SNP	Chromosome	Genes
rs2269688	8	MTMR7
rs11259403	10	PRKCQ
rs13389996	2	CTNNA2
rs10778462	12	CKAP4
rs7136826	12	CLEC1A
rs11632584	15	MEGF11
rs7163369	15	SLCO3A1
rs732523	12	PCED1B
rs17276467	7	CREB3L2
rs10209276	2	KCNH7
rs4578863	2	ZC3H6

Unfortunately, the SNP found to be mostly significant associated with anemia (Fig. 2) at chromosome 3 and 7 have not been annotated hence the functions are not known.

RESULTS AND DISCUSSION

Fig. 3 : Interactions between genes which showed significant association with anemia.



❖The SNPs that significantly associated with anemia are found in the genes that are co-expressed (Table. 1, Fig. 3), their functions are associated with immune response, hindbrain development and central nervous system neuron differentiation in humans.

❖The immune response is activated by frequent infections that individuals with SCD often experience.

Conclusion and future work

- This study indicated genetic markers (SNPs) that associate with anemia in individuals with SCD in Tanzania.
- It is an important step towards developing a tool that will quickly identify the variants linked to anemia in individuals SCD.
- The completion of imputation and replication work will hopeful reveal more and significant associations.
- In order to confirm the variants, we recommend similar analysis to be conducted in same and other cohorts of SCD.

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