Investigating MicroRNAs as a Biomarker for Analyzing Racial and Gender Disparities in B-cell ALL Patients

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Introduction

Leukemias are hematologic malignancies. They develop due to failures in the process that creates normal leukocytes, causing an accumulation of immature, dysfunctional cells. Leukemias are the eleventh leading cause of cancer deaths globally, and there are currently 376,508 leukemia patients either living with the disease or are in remission nationally. B-cell acute lymphoblastic leukemia is caused by an excess of B lymphoblasts malignancies in the bone marrow.

Evidence reveals that miRNAs can be used as biomarkers in order to examine the early stages of leukemia and view the impact of chemotherapy on the progression of the disease. Specifically in acute myeloid leukemia, miRNA has been found to impact all parts of the progression of AML development: including a patient's survival rate, the differentiation in the progression of their disease, and cell proliferation. Gender disparities in leukemia have not yet been well-studied; males are affected more by leukemia than females. In chronic myeloid leukemia, women are typically diagnosed at a later stage and have lower platelet counts compared to men. However, when diagnosed, men are found to have higher hemoglobin levels, a larger spleen size, and abnormalities in gene expression. In all blood cancers, White patients are diagnosed more frequently, yet Black and Hispanic patients with AML have a worse survival rate. We aim to analyze miRNA expression in B-cell ALL using the publicly available data set from Tumor Cancer Genome Atlas (TCGA), a public genomic database with the intention to advance cancer research. Due to the limitation of our data set, we limit our analysis among male and female, and Hispanic and non-Hispanic patients. The result of this project will help us to determine miRNA signatures as a biomarker to examine racial and gender disparities in B-cell acute lymphoblastic leukemia.

Methods

- We downloaded the B-cell ALL patient data from publicly available TCGA dataset (https://portal.gdc.cancer.gov/).
- Data was then analyzed by "Multivariate analysis-based gene shaving," which uses the influence function of canonical correlation analysis [PMID: 31120939] and was implemented by an RKUM R-packages.

Results

Patient Demographics

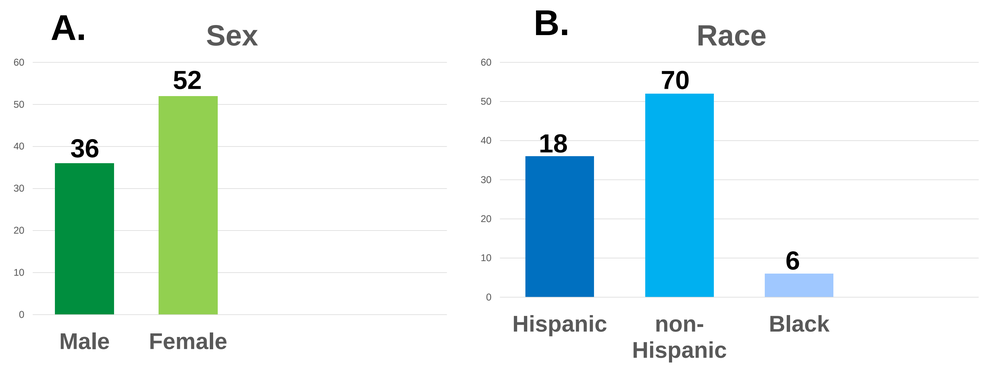

Figure 1. The race and sex demographics of the B-cell ALL patient data set (n=88). A) The table displays the demographics of the B-cell ALL patients in our data set; there are 36 male and 52 female patients. B) The table illustrates the race demographics of the B-cell ALL patients; there are 18 Hispanic or Latino patients, 70 non-Hispanic or Latino (White) patients, and 6 Black patients recorded.

Canonical Correlation Analysis

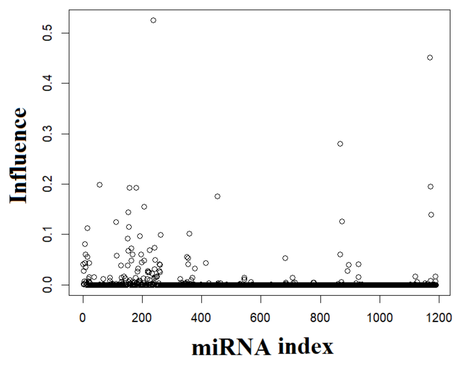

Figure 2. The influence function of canonical correlation analysis between Hispanic and non-Hispanic B-cell ALL patients' miRNAs.

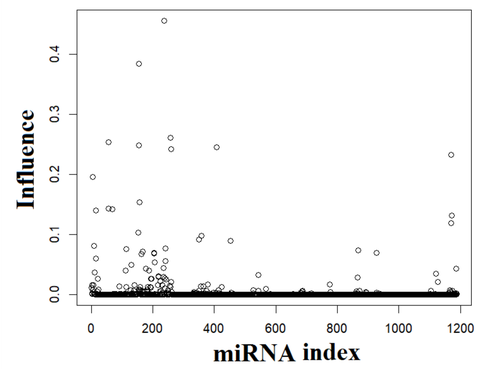

Figure 3. The influence function of canonical correlation analysis between male and female B-cell ALL patients' miRNAs.

Differential Expression of miRNA

hsa-let-7a-1	hsa-mir-1287
hsa-let-7a-2	hsa-mir-129-2
hsa-let-7a-3	hsa-mir-1307
hsa-let-7b	hsa-mir-130a
hsa-let-7c	hsa-mir-130b
hsa-let-7d	hsa-mir-140
hsa-let-7e	hsa-mir-142
hsa-let-7f-1	hsa-mir-143
hsa-let-7f-2	hsa-mir-145
hsa-let-7g	hsa-mir-146a
hsa-let-7i	hsa-mir-148b
hsa-mir-101-1	hsa-mir-150
hsa-mir-103a-1	hsa-mir-151a
hsa-mir-103a-2	hsa-mir-15a
hsa-mir-106a	hsa-mir-15b
hsa-mir-106b	hsa-mir-16-1
hsa-mir-107	hsa-mir-16-2
hsa-mir-10a	hsa-mir-17
hsa-mir-10b	hsa-mir-181a-1
hsa-mir-122	hsa-mir-181a-2
hsa-mir-1247	hsa-mir-181b-1
hsa-mir-125a	hsa-mir-181b-2
hsa-mir-125b-2	hsa-mir-181d
hsa-mir-128-1	hsa-mir-182
hsa-mir-128-2	hsa-mir-183

Table 1. The top 50 miRNAs significantly associated with Hispanic and non-Hispanic B-cell ALL patients. We identified 157 significant miRNAs out of 1188 miRNAs in the dataset.

hsa-let-7a-1	hsa-mir-140
hsa-let-7a-2	hsa-mir-141
hsa-let-7b	hsa-mir-142
hsa-let-7c	hsa-mir-143
hsa-let-7d	hsa-mir-145
hsa-let-7e	hsa-mir-146a
hsa-let-7f-1	hsa-mir-148b
hsa-let-7g	hsa-mir-150
hsa-let-7i	hsa-mir-151a
hsa-mir-100	hsa-mir-155
hsa-mir-103a-1	hsa-mir-15b
hsa-mir-103a-2	hsa-mir-16-1
hsa-mir-106b	hsa-mir-16-2
hsa-mir-10a	hsa-mir-17
hsa-mir-10b	hsa-mir-181a-1
hsa-mir-1247	hsa-mir-181a-2
hsa-mir-1248	hsa-mir-181b-1
hsa-mir-125a	hsa-mir-181b-2
hsa-mir-1266	hsa-mir-181c
hsa-mir-128-1	hsa-mir-182
hsa-mir-1306	hsa-mir-183
hsa-mir-1307	hsa-mir-186
hsa-mir-130a	hsa-mir-18a
hsa-mir-130b	hsa-mir-18b
hsa-mir-132	hsa-mir-191

Table 2. The top 50 miRNAs where the most variation exists between male and female B-cell ALL patients. We found 163 significant miRNAs out of 1188 miRNAs in the dataset.

Conclusions

- We identified significant differential miRNA expression based on sex and race in B-cell ALL patients.
- Significant miRNA interaction exists between male and female as well as Hispanic and non-Hispanic patients.
- **In summary, candidate B-cell ALL biomarkers based on miRNA signatures should take into account sex and ethnicity differences.**

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