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

A. Sex

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>36</td>
<td>52</td>
</tr>
</tbody>
</table>

B. Race

<table>
<thead>
<tr>
<th></th>
<th>Hispanic</th>
<th>non-Hispanic</th>
<th>Black</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td>18</td>
<td>70</td>
<td>6</td>
</tr>
</tbody>
</table>

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.

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.

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.

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.

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