Expression of microRNA Change after Chemotherapy in Breast Cancer Patients

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Introduction

- **Breast Cancer continues to be the second leading cause of cancer related death in women in the United States only after lung cancer[1]**
- **Even with early detection and new treatments, some patients, unfortunately, have further progression of disease even on definitive treatment or have a recurrence of their cancer within a short period of time**
- **There continues to be a need for new targets for therapy and new markers for early identification of disease or monitoring treatment success**
- **MicroRNAs (miRNA), small non-coding RNAs, function in gene regulation and proper cell function**
- **In vitro experiments have linked miRNAs including 23b, 27b, and let-7a to breast cancer metastasis and may play a role in the pathogenesis and progression of cancer**
- **Our lab has recently shown there was increased miRNA expression of let-7a and 125a in patients with breast cancer compared to controls without any known cancer**
- **In this study, we look to examine the differential expression of miRNA before chemotherapy and after definitive treatment**
- **We hope to identify molecular markers that may serve as molecular markers to identify early recurrence of disease which may help patients make informed decisions about their treatment options**

Study Design

- **Several newly diagnosed breast cancer patients were recruited between April 2021 to December 2022 at the University Medical Center New Orleans**
- **Plasma samples were collected at diagnosis and after their last chemotherapy treatment**
- **We extracted total RNA from plasma using Qiagen miRNeasy Serum/Plasma Advanced Kit**
- **The expression of the microRNA (miR-125-3p, 23b, 27b, let-7a, 192-5p, 451a) was measured using qRT-PCR with the TaqMan small RNA assay method**
- **Expression levels were analyzed based on each sample's CT value**
- **The samples were compared using paired sample t-test with p-value of < 0.05 considered statistically significant**

Results

Figure 1: Heatmap comparing relative expression of the genes of interest for each patient analyzed. Lighter colors correlate with increased expression of the microRNA in circulating plasma of breast cancer patients' post-chemotherapy compared to their baseline plasma at diagnosis. Figure shows miR-let-7a and miR-125a-3p with increased expression comparatively to the other genes of interest

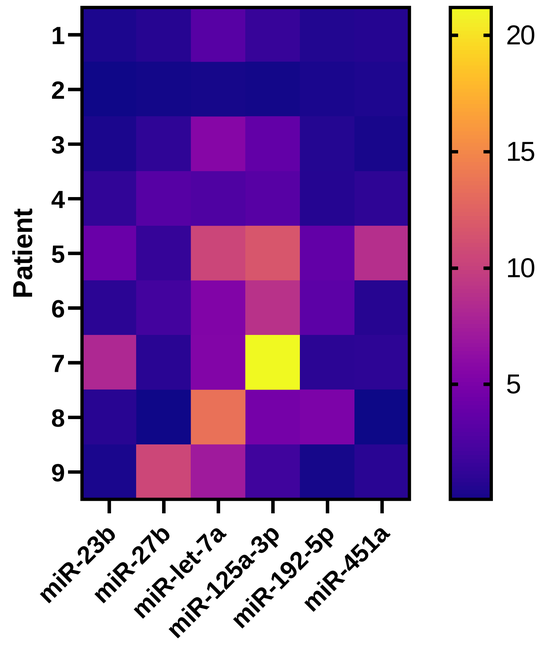
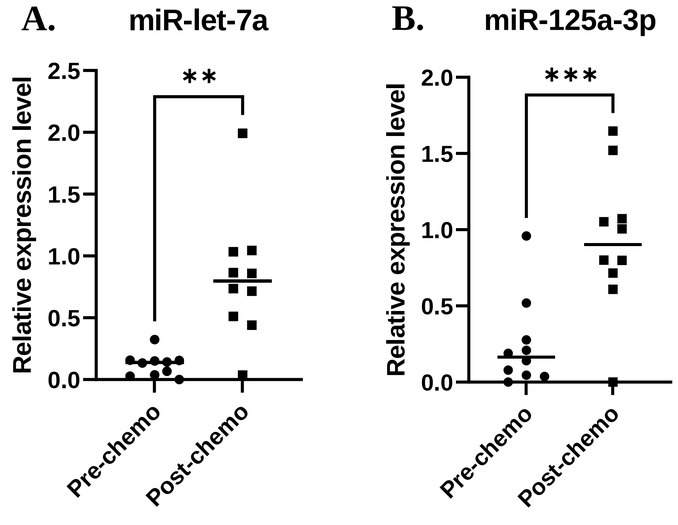


Figure 2: A. Significant increase in expression of miR-let-7a after treatment with chemotherapy with a p-value of < 0.0018 **B.** Significant increase in expression of miR-125a-3p after treatment with chemotherapy with a p-value of <0.0003



Discussion

- **Circulatory miRNAs represent the potential to serve as diagnostic biomarkers, markers for molecular identification of residual disease, stratification of risk of recurrence and monitoring of treatment**
- **We found significant increase in expression of miR-let-7a and miR-125a-3p after definitive treatment with chemotherapy**
- **miR-let-7a is downregulated in numerous types of cancer including breast cancer and acts as a tumor suppressor by regulating the expression of RAS and HMGA2 oncogenes[2]**
- **Decreased levels of miR-let-7a was found to be associated with elevated RAS, an oncogene which promotes tumor cell grown [2]**
- **With increased miR-let-7a, there is downregulation of breast cancer cell invasion and migration[2]**
- **miR-125a-3p also functions as a tumor suppressor by regulating the BRCA1 signaling[3]**
- **Overexpression of miR-125a down-regulates HER2 thereby reducing the cells' migration and invasion capabilities[4]**
- **Increased expression of both miR-Let-7a and miR-125a-3p in our patient population is promising by showing treatment with chemotherapy results in increased expression innate tumor suppressors**
- **The role of miRNAs expression after chemotherapy should be further explored with a larger patient population**

Future Directions

- **We plan to expand our study to include a larger patient population including patients from another institution**
- **We also plan to start to explore the differential expression of miRNA in paraffin tissue sections and how it differs from plasma samples**
- **We will further explore expression of miRNA in patients before and after definitive treatment with surgery**

References

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