Circulating miRNA Biomarkers in Early Breast Cancer Detection Following Mammography

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Introduction

The currently accepted stepwise model of breast tumorigenesis assumes a gradual transition from normal breast epithelial cells to atypical ductal hyperplasia (ADH), to ductal carcinoma in situ (DCIS), and then to invasive ductal carcinoma (IDC). Percutaneous core needle biopsy (CNB) is the standard technique following an abnormal mammographic finding. However, CNB is less reliable in differentiating simple ADH (sADH) from ADH component coexisted with advanced lesions such as DCIS and/or IDC (cADH). Therefore, to identify and validate novel reliable molecular biomarkers is essential in order to improve the efficiency of therapeutic recommendations, as well as to minimize anxiety and unnecessary procedures. Our lab has recently characterized two important miRNAs, miR-671-5p and miR-638, that are involved in breast cancer progression.

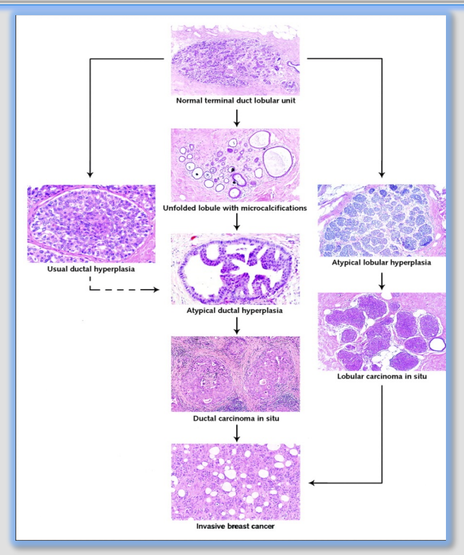

Figure 1: Linear Progression of Breat Tumorigenesis (Arpino G, Laucirica R, Elledge RM. Premalignant and In Situ Breast Disease: Biology and Clinical Implications. Ann Intern Med. 2005;143:446-457. doi: 10.7326/0003-4819-143-6-200509200-00009)

Objectives

The goal of this research is to analyze and validate the candidate miRNAs that may differentiate sADH from cADH using FFPE and blood samples following mammography.

Materials & Methods

Microdissection and Total RNA isolation from FFPE samples. FFPE blocks were microdissected, with each sample containing normal, ADH, DCIS, and IDC tissue. Total RNA was isolated using the *RecoverAll*™ Total Nucleic Acid Isolation Kit.

Collection of patients' blood and Total RNA isolation before CNB procedure. Following IRB protocol, patients with lesions detected on mammography elected to donate a blood sample. miRNA was isolated using *Purelink*™ miRNA Isolation Kit

Examination of miRNA expression by qRT-PCR: qRT-PCR was performed to determine the gene expression of both the FFPE samples and the blood samples.

Results

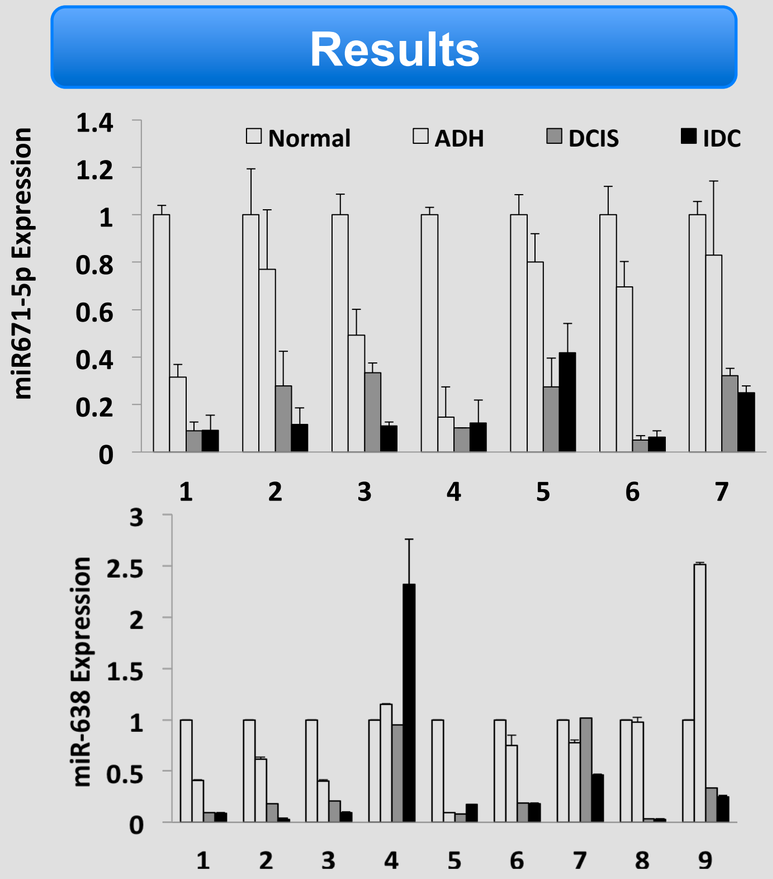

Figure 2. Expression of miR-671-5p and miR-638 during breast cancer progression using microdissected FFPE samples. miR-671-5p and miR-638 were consistently down-regulated in ADH, DCIS, and IDC vs. normal controls.

Results

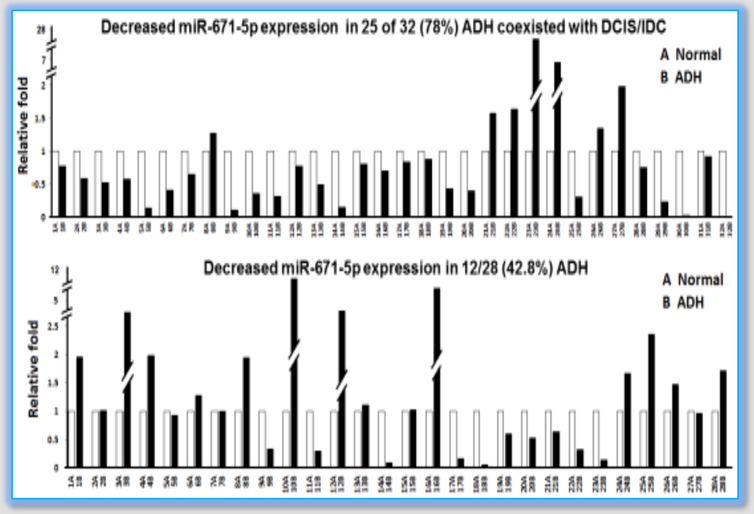

Figure 3. Differential expression pattern of miR-671-5p between sADH and cADH. miR-671-5p expression was decreased in 78% of sADH cases.

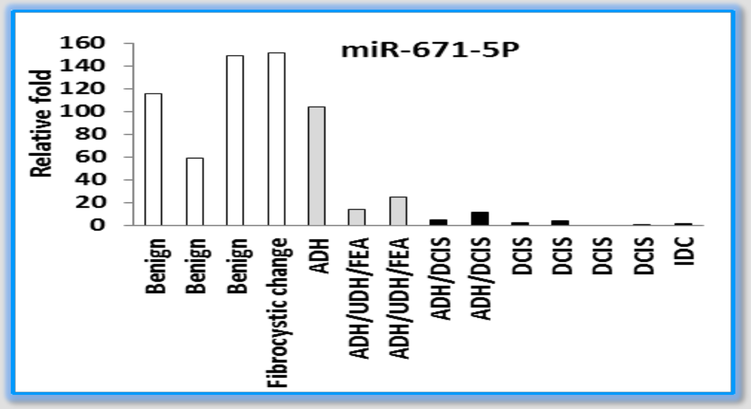

Figure 4. Expression of miR-671-5p in serum from ADH cases diagnosed by CNB.

Conclusions

Our data suggest that miRNAs, such as miR-671-5p and miR-638, may be potential circulating biomarkers for early breast cancer detection following mammography and CNB.