Differential Expression of miR-21, miR-205, miR-221, miR-222, and miR-150 in Molecular Subtypes of Breast Cancer

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Differential Expression of miR-21, miR-205, miR-221, miR-222, and miR-150 in Molecular Subtypes of Breast Cancer

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Background

microRNAs (miRNAs) are short RNA molecules that are involved in many critical cellular processes including oncogenesis. Different cancer types and subtypes at different stages of progression display unique miRNA profiles that may be used as diagnostic, prognostic and therapeutic tools. The detection of miRNA in clinical samples has been difficult, requiring total RNA extracts which lack critical spatial information. In situ hybridization (ISH) allows direct assessment of malignant cells. Evaluation of miRNA profiles in breast cancer (BR CA) holds promise for improving understanding of pathogenesis and therapeutic outcome. This pilot study is designed to assess the feasibility of miRNA profiling in formalin fixed paraffin embedded (FFPE) BR CA samples using in-situ hybridization (ISH) for miR-150, -21, -205, -221 and -222 immunostains.

Design

18 samples of FFPE BR CA and 10 normal breast samples were studied. BR CA were molecularly subtyped using immunostains for Estrogen Receptor, Progesterone Receptor, and HER-2/neu (all BioGenex). Sub categorization resulted in 5 ER/PR positive (+), 5 Her2+, and 8 triple negative (TN) BR CA. Cases were subjected to ISH using FAM-labeled microRNA probes (BioGenex) followed by Super Sensitive ISH Detection Kit (BioGenex, DF400-YAX). Scramble probes served as negative control.

Results

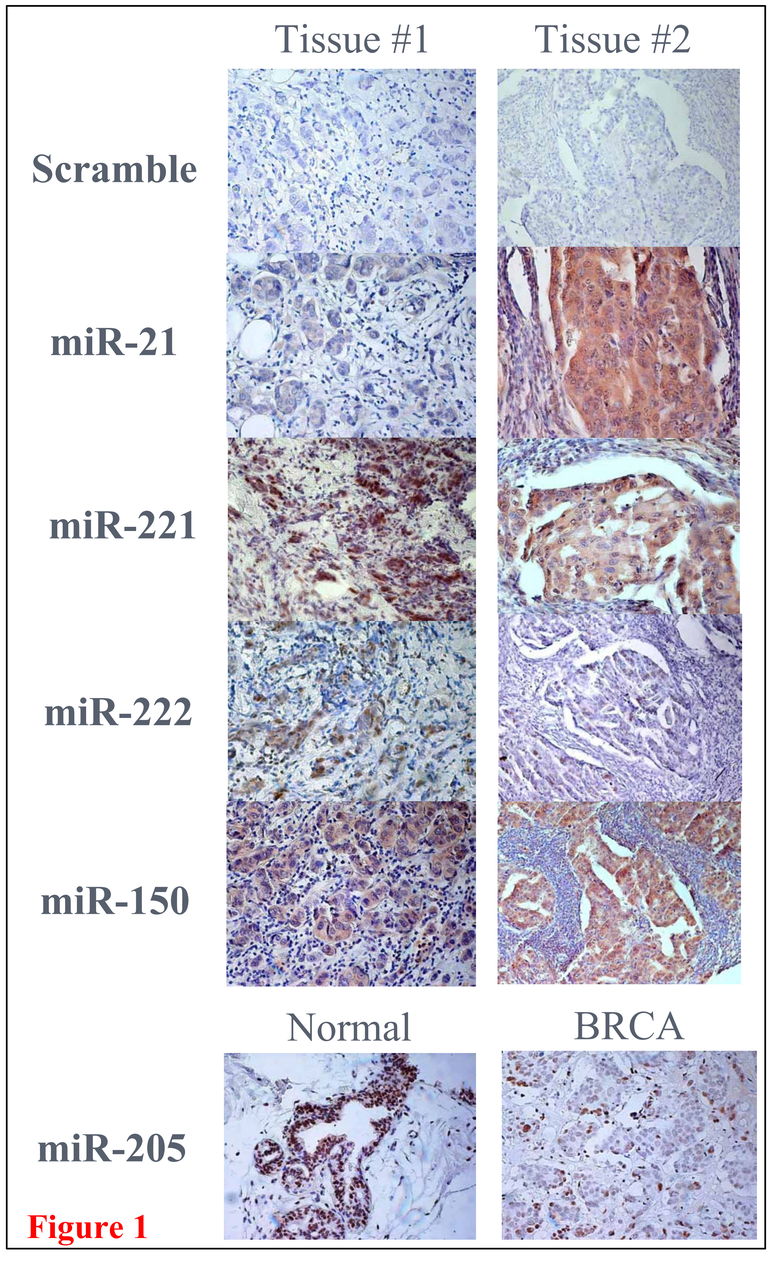

Figure 1

Results

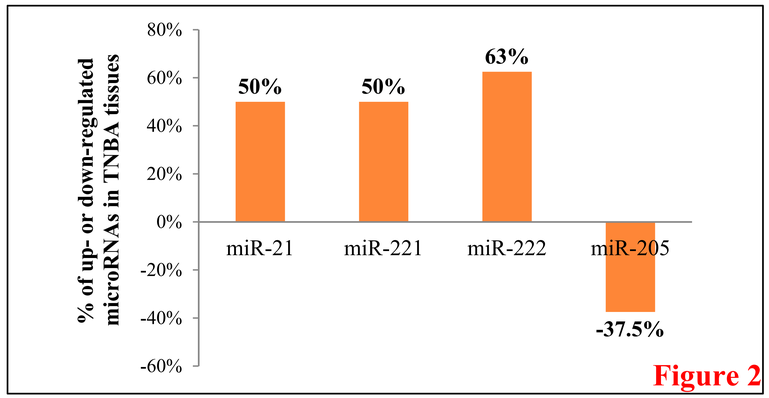

Figure 2

Figure 1. The staining of representative normal and breast cancer tissues using microRNA probes.
Figure 2. The percentage of up-regulated miR-21, miR-221, and miR-222, as well as down-regulated miR-205 in TN BR CA.

TN BR CA showed up-regulation of miR-21 (2/4 cases), miR-221 (4/8 cases), miR-222 (5/8 cases) and down-regulation of miR-205 (3/8 cases). miR-150 was up-regulated in Her2+ BR CA but reduced in ER/PR+ BR CA. Normal breast tissue showed low to negative.

Conclusion

miRNA profiling is feasible in FFPE samples of BR CA using chromogenic ISH. Although no significant difference was noted in the expression of the various miRNAs in the different molecular subtypes, the presence of differential staining warrants additional studies on larger number of cases to determine prognostic/predictive value.