OVEREXPRESSION OF MIR-155 DISRUPTS ER SIGNALING IN MCF-7 BREAST CANCER CELLS.

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microRNAs (miRNA) are short non-coding RNAs that regulate gene function through translational inhibition. Changes in miRNA expression patterns have been linked to diseases such as cancer and differences in miRNA expression profiles have been shown to correlate with breast cancer receptor status, including receptors estrogen receptor (ER), progesterone receptor (PgR), and c-erbB-2 (HER2/Neu). Here we demonstrate differences in miRNA expression patterns between ER – and ER + breast cancer cell lines. Specifically we show that miR-155 expression is upregulated in the ER – breast cancer cell lines. Furthermore we show that ectopic expression of miR-155 in the ER + MCF-7 breast cancer cells results in a deregulation in the ER signaling pathways both in vivo and in vitro. Notably overexpression of miR-155 leads to changes in the expression patterns of ER regulated genes by decreasing PGR and SDF-1 mRNA basal levels and increasing SERPINA3 and BCL2 mRNA basal levels. A suppression of estrogen-stimulated clonogenicity and tumorigenesis is also observed in MCF-7 cells overexpressing miR-155. In vitro overexpression of miR-155 drives MCF-7 cells towards a PgR – and ER + phenotype that is suggestive of a hormone independent phenotype observed in clinical tumor samples. This hormone independence is further observed in vitro through the decreased clonogenicity of MCF-7 cells overexpressing miR-155 following E2 treatment when compared to vector control cells. In vivo hormone independence is observed through decreased tumor size in MCF-7 tumors overexpressing mature miR-155 following treatment with 17beta estradiol. Taken together our data demonstrates a role for miR-155 in ER signaling in MCF-7 breast cancer cells and suggests miR-155 may play a role in establishing hormone independence in this cell line.