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The EGFR Signaling Modulates in Mesenchymal Stem Cells the Expression of miRNAs Involved in the Interaction with Breast Cancer Cells

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Abstract

We previously demonstrated that the epidermal growth factor receptor (EGFR) modulates in mesenchymal stem cells (MSCs) the expression of a number of genes coding for secreted proteins that promote breast cancer progression. However, the role of the EGFR in modulating in MSCs the expression of miRNAs potentially involved in the progression of breast cancer remains largely unexplored. Following small RNA-sequencing, we identified 36 miRNAs differentially expressed between MSCs untreated or treated with the EGFR ligand transforming growth factor α (TGFα), with a fold change (FC) < 0.56 or FC ≥ 1.90 (CI, 95%). KEGG analysis revealed a significant enrichment in signaling pathways involved in cancer development and progression. EGFR activation in MSCs downregulated the expression of different miRNAs, including miR-23c. EGFR signaling also reduced the secretion of miR-23c in conditioned medium from MSCs. Functional assays demonstrated that miR-23c acts as tumor suppressor in basal/claudin-low MDA-MB-231 and MDA-MB-

468 cells, through the repression of IL-6R. MiR-23c downregulation promoted cell proliferation, migration and invasion of these breast cancer cell lines. Collectively, our data suggested that the EGFR signaling regulates in MSCs the expression of miRNAs that might be involved in breast cancer progression, providing novel information on the mechanisms that regulate the MSC-tumor cell cross-talk