Effect of miR-660-5p in breast cancer progression

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Background: Breast cancer (BC) is the most diagnosed cancer in women worldwide. MicroRNAs (miRNAs) participate in different processes of BC and their deregulation can cause them to act as oncogenes or tumor suppressors, participating in cancer progression. Using the TCGA (The Cancer Genome Atlas) database, we found that miR-660-5p significantly overexpressed and associated with poor survival in patients with this pathology. Moreover, it is reported that miR-660-5p can induce BC progression through transcription factor CP2 (TFCP2) and the downregulation of tet methylcytosine dioxygenase 2 (TET2). In this project, we propose to identify the role of miR-660-5p in proliferation, migration, invasion, angiogenesis, and the possible targets involved in these processes in BC cell lines.

Methods: Basal levels of miR-660-5p were determined in BC cells MDA-MB-231 and MCF-7, and in human epithelial breast cells MCF-10A by RT-qPCR. The effect of miR-660-5p was evaluated on proliferation, migration, and invasion processes in MDA-MB-231 and MCF-7 cells. HUVEC cells were used to assess angiogenesis. All cell lines were transfected with miR-660-5p inhibitor. Analysis of nine miRNA-target prediction databases was made to identify targets of miR-660-5p. We selected the targets genes predicted by at least three of these programs, and their expression were evaluated in MDA-MB-231 cells by RT-qPCR in a customized plate. We validated those results with Western blot.

Results: We found that miR-660-5p is significantly upregulated in MDA-MB-231 and MCF-7, compared to MCF-10A cells. In addition, we observed a significant decrease in proliferation, migration, and invasion in BC cells transfected with miR-660-5p inhibitor, compared to nontreated cells and miRNA inhibitor negative control cells. Similarly, we observed a significant decrease in angiogenesis of HUVEC cells transfected with miR-660-5p inhibitor. Furthermore, of all the miR-660-5p target genes identified by prediction databases, 17 were selected, and of these, three were observed upregulated and one downregulated. We found that CD8A, LIFR and TMEM41B are reported as tumor suppressors in different types of cancer. We validated those results by Western blot, observing an increase in TMEM41B protein levels in the group of cells transfected with miR-660 inhibitor compared to nontreated cells and miRNA inhibitor negative control cells.

Conclusions: The results show that miR-660-5p is upregulated and involved in proliferation, migration, invasion, and angiogenesis of BC, which may lead us to suggest that this miRNA act as an onco-miRNA. In addition, we found that TMEM41B could be a potential target of miR-660-5p.