THERAPEUTIC POTENTIAL OF LET-7, MIR-125, MIR-205, AND MIR-296 IN BREAST CANCER: AN UPDATE

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ABSTRACT

In 2008, first time we hypothesized that Let-7, miR-125, miR-205, and miR-296 may be potential next-generation therapeutics in breast cancer. In recent years, various reports have supported our hypothesis and it seems that in near future these miRs are highly likely to be used for breast cancer therapy. This commentary summarized the recent findings towards establishing our report of 2008.

Key words: Breast cancer; cancer therapy; miRNA; molecular medicine

COMMENTARY

In 2008 we reported that Let-7, miR-125, miR-205, and miR-296 could be potential therapeutics in breast cancer [1]. In that work we had shown, Let-7 could target estrogen receptor, mitogenic, and angiogenic signaling pathways and thereby blocks cell cycle, cell proliferation, cell migration, angiogenesis, and metastasis in breast cancer. For miR-125, miR-205, and miR-296, we had predicted that, these miRs can precisely inhibit various growth receptor signaling cascades and positive regulators of cell cycle.

The current experimentally validated knowledge of these four miRs in respect to breast cancer supports our hypothesis of 2008 [1]. Let-7 based therapeutic approaches in lung cancer [2] had already been established before our report. However, several validation reports after our publication in 2008 strongly suggest that Let-7 will also be an effective therapeutic in breast cancer. Let-7 is a tumor suppressor miRNA and is downregulated in breast cancer [3]. Whereas, Let-7b inhibits estrogen receptor signaling [4], induces TP53 mediated apoptosis [5]; Let-7a and Let-7d reported to inhibit cell cycle and cell proliferation [6-7]. Chang et al in 2011 have showed that Let-7d prevents epithelial to mesenchymal transition and cell migration [8]. Further, Zhao et al (2011) reported that downregulation of Let-7d makes breast cancer resistance to tamoxifen [4]. The latest report reveals that, Ectopic expression of Let-7b inhibits cell migration in breast cancer [9]. Therefore, administration of Let-7 miRNA might be a future therapeutic in drug registrant and estrogen positive metastatic breast cancers.

Similar to the Let-7; miR-125 is a putative tumor suppressor miRNA and miR-125a-5p is downregulated in ductal breast cancers [10]. Mutation in the miR-125a-5p gene is reported to be associated with hereditary breast cancers [11]. This miRNA inhibits cell proliferation, cell migration, and induces apoptosis also [12-13]. The third miRNA we identified in 2008 was miR-205 [1]. According to Song and Bu (2009) miR-205 inhibits cell migration [14]. miR-205 is downregulated in breast cancer [3] and induced expression inhibits cell proliferation in breast cancer [15]. It also makes the breast cancer cells susceptible to Lapatinib [16]. The last miRNA we reported was miR-296. This miRNA later reported to be involved in regulation of apoptosis [17] and negative regulation of cell migration [18]. Further, Vaira et al (2012) also showed that this miR-296 is downregulated in breast cancer and its ectopic expression inhibits cell proliferation in breast cancer [18].

CONCLUSION

Last four year’s (2008-2012) experiments by various research groups suggest that our proposed Let-7, miR-125, miR-205, and miR-296 based therapeutics in breast cancer [1] could be recognized in near future. Let-7 based Lung cancer therapy is already at clinical trial level. The cell cycle, cell proliferation, cell migration, angiogenesis, and metastasis inhibitory effects of these four miRNAs in breast cancer cells have now been established by various researchers after our report in 2008. We hope that, very soon these miRNAs will enter into clinical trial towards establishing them as next-generation breast cancer therapeutics.
REFERENCES


