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Molecular Modulation of miRNA Expression: New Strategy for Breast Cancer Treatment

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ABSTRACT

The tumor suppressive miR-34a is shown to inhibit breast cancer cell proliferation as well as being a marker of increased disease free survival. Polydatin (PD) derived from *Polygonum cuspidatum* are phytochemicals with anti-tumorigenic properties however, little is known about the miR-34a role in their mechanism of action. The present study investigated the potential influence of PD on breast cancer generally and on miR-34a signaling specifically, wherein, human breast cancer cells ER+ (T-47D) or TNBC (MDA-MB-231) were treated with a concentration range of PD. Cell proliferation was subsequently evaluated by WST-1 assay that displays an inhibition in cell proliferation and viability in a dose-dependent way. The results also showed that PD induces apoptosis as indicated by stimulation of histone release from fragmented DNA, caspase-3 activity, and cell shrinkage. QRT-PCR and western blot analysis of extracted RNA and total protein revealed the up-regulation of miR-34a expression in response to PD treatment which correlated with the down-regulation of miR-34a target gene, SIRT. Moreover, PD treatment showed a significant reduction in STAT3, β-catenin and mutant p53 levels as well as an elevation in STAT5 and PPARγ levels in both examined cell lines. Taken together, our data suggested the potential therapeutic value of PD as promising anti-breast cancer agent and implicated miR-34a as a key component of PD anti-proliferative activity.