LINC00266-1 is associated with tocotrienol-rich fraction cytotoxicity in triple-negative breast cancer cells

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ABSTRACT

Introduction: Triple negative breast cancer (TNBC) is a highly aggressive and heterogeneous subtype of breast cancer that lacks targeted therapies. Tocotrienol-rich fraction (TRF), a vitamin E derivative, has demonstrated potent anticancer properties in both in vitro and in vivo models and is a promising therapeutic agent. However, its molecular mechanisms remain poorly understood. Meanwhile, long non-coding RNAs (lncRNAs) have emerged as critical regulators of various biological processes. While some studies have explored TRF's effects on microRNAs, the role of lncRNAs in mediating TRF's anticancer effects has not been investigated. While some studies have focused on TRF's effects on microRNAs, the potential roles of lncRNAs in mediating TRF's anticancer effects have not been investigated. Aims: This study investigates the regulatory roles of lncRNAs in TRF-treated TNBC cells. **Materials and Methods:** MDA-MB-468 cells were treated with TRF (17 µg/ml, 72 hours), and transcriptomic profiling was performed using the Clariom™D microarray. Differentially expressed genes were identified (fold change > 2, $p < 0.05$) and then used to construct co-expression lncRNA-mRNA pairs (Pearson's correlation, $|r| > 0.99$, $p < 0.05$). Functional enrichment of the co-expressed mRNAs was carried out using the Reactome Pathway database, and hub lncRNAs were identified using cytoHubba (Maximal Clique Centrality [MCC] algorithm). **Results:** TRF treatment significantly altered the expression of 530 lncRNAs (278 upregulated, 252 downregulated) in TNBC cells treated with TRF compared to untreated controls. Co-expression analysis revealed 5259 significant lncRNA-mRNA pairs, with enriched pathways including "Cell Cycle Mitotic", "Cell Cycle Checkpoints" and "DNA Replication". In addition, network analysis identified LINC00266-1 as a top hub lncRNA, correlating with 12 cell cycle genes (ANAPC11, CTNNB1, EXO1, FOXM1, KIF14, KIF23, KIF2C, MAPRE1, MCM2, PCNA, TPX2, ZWINT) **Conclusion:** Overexpression of LINC00266-1 is associated with the modulation of cell cycle related genes and TRF-induced cytotoxicity in MDA–MB–468 cells.

Keywords: Triple negative breast cancer, long non coding RNA, tocotrienols