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Inhibition of TP53 Suppressor MiRNAs in Human Breast Cancer: A Bioinformatic Approach for Anti-miRNA Oligonucleotide Design

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ABSTRACT

Introduction: Tumor protein p53 (*TP53*), a pivotal tumor suppressor gene, is known to exhibit decreased expression in breast cancer. One crucial mechanism involved in the downregulation of *TP53* expression is the targeted binding of miRNAs to TP53 mRNA. Antisense oligonucleotides (AMOs) have emerged as potential therapeutic agents for targeting dysregulated miRNAs in various human pathologies, including cancer. Chemically modified AMOs, such as locked nucleic acid oligonucleotides, have effectively silenced miRNAs and modulated their functional activities. This research aimed to design AMOs that can effectively suppress the miRNAs responsible for downregulating *TP53* gene expression in breast cancer.

Methods and Materials: Bioinformatics tools, including miRNA target prediction and functional annotation database, including TargetScan, miRTarBase, and Mirwalk, were used to identify miRNA targets for *TP53*. The association of *TP53* with related genes was confirmed through analysis using DisGeNET and Norwalk. A comprehensive gene network was constructed using GeneMANIA to elucidate the functional relationships among these genes. The selection and analysis of AMOs were conducted using NCBI resources for target identification and characterization.

Results: The analysis identified hsa-miR-150-5p as a specific miRNA targeting 10 TP53 variants. In addition to *TP53*, hsa-miR-150-5p exhibited targeting capabilities towards *EGR2*, *ZEB1*, *PRKCA*, *SP1*, *MYB*, *NR2F2*, *GOSR1*, *VPS53*, *EPHB2*, *MMP14*, and *ADIPOR2* genes. Among the identified AMOs, the Mir AMO with the sequence CTGTCCCCCAGGCCTGTACCA was selected for further analysis.

Conclusion and Discussion: The findings underscore the importance of well-designed AMOs in effectively targeting specific miRNAs. Strategies such as improving nuclease resistance and enhancing target affinity contribute to optimizing the therapeutic potential of AMOs. AMO therapy holds promise in the reduction and treatment of breast cancer. However, further clinical trials are necessary to validate the efficacy and safety of this approach.

Keywords: Breast neoplasms, MicroRNAs, TP53 protein