Effect of Transitive RNAi on Gene Expression in Human Cells

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This project investigates potential of transitive RNAi in human genetic modification, a phenomenon currently discovered only in viruses, bacteria, and plants. Transitivity allows gene-specific siRNA to continuously degrade mRNA beyond an initial target gene by independently assembling templates of subsequent gene sequences. Due to its versatility and efficiency, harnessing transitive RNAi mechanisms for extensive targeting mRNAs of disease-related genes may revolutionize personalization of almost all disease treatment from AIDS to Huntington's Disease. To determine possibility of transitive RNAi transitivity, a novel approach employed siRNA which target both artificially transfected and inherent gene sequences in variant and full-length PTEN and ARFL genes. 293FT cell cultures were transfected with target-specific siRNA and assessed with Western Blot tests for protein detection. Initially, siRNA targeting a unique codon in the oncogene ARV7 failed to decrease gene expression of the identical, but target codon-less, full-length ARFL sequence. However, in cells with PTEN sequences transfected with artificial GFP targets, nonGFP fused PTEN expression also drastically decreased, suggesting weak possibility successful transitivity. Therefore, the efficacy of using RNAi in viable cell environments as a genetic modifier is strongly supported by the Western Blot Test results, although a definitive ruling on the viability of transitive RNAi in human cells is currently inconclusive and requires further investigation of its mechanisms.

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