Cell-Based Delivery of Gene-Silencing Products via Gap Junction Channels

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MicroRNAs (miRNA) are small non-coding RNA molecules, approximately 19-25 nucleotides in length, which function in post-transcriptional regulation of gene expression by base-pairing with targeted mRNA, resulting in a gene-silencing effect. It has been shown that miRNAs have tumor suppressive effects in an array of human cancers and are able to be passed through intercellular gap junction channels; however, a specific and efficient delivery system remains the largest impediment to therapeutic applications. This study investigated the regulatory effects of microRNA-16 (miR-16) in human prostate cancer cells (PC3) and the potential of a miRNA delivery system from adult human bone marrow-derived mesenchymal stem cell (hMSC) donor cells to recipient PC3 cells. Results showed that miR-16 was a significant regulator of PC3 cell growth as miR-16 transfected PC3s experienced the onset of a round morphology, decreased proliferation, and downregulation of BCL-2, an anti-apoptotic protein. After the regulatory impact of miR-16 on PC3s was demonstrated in monoculture, co-culture of the two cell types showed that the hMSCs successfully delivered miR-16 to recipient PC3s with the regulatory effects preserved. Additionally, data analysis of in vivo procedures which were performed by lab personnel offered proof-of-concept of in vitro results. This study presents a preliminary model for therapeutic applications of a cell-based microRNA delivery system in cancer.

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