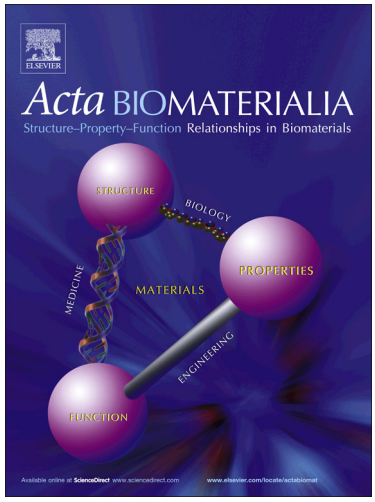

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miRNA oligonucleotide and sponge for miRNA-21 inhibition mediated by PEI-PLL in breast cancer therapy

Shiqian Gao[a,c], Huayu Tian[a], Ye Guo[b], Yuce Li[a], Zhaopei Guo[a], Xiaojuan Zhu[b,*] , Xuesi Chen[a, *]

[a] *Key Laboratory of Polymer Ecomaterials, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, China*

[b] *School of Life Science, Northeast Normal University, Changchun 130024, China*

[c] *Graduate School of Chinese Academy of Sciences, Beijing 100039, China*

ABSTRACT

MicroRNA-21 (miR-21) inhibition is a promising biological strategy for breast cancer therapy. However its application is limited by the lack of efficient miRNA inhibitor delivery systems. As a cationic polymer transfection material for nucleic acids, the poly (*L*-lysine)-modified polyethylenimine (PEI-PLL) copolymer combines the high transfection efficiency of polyethylenimine (PEI) and the good biodegradability of polyllysine (PLL). In this work, PEI-PLL was successfully synthesized and confirmed to transfect plasmid and oligonucleotide more effectively than PEI in MCF-7 cells (human breast cancer cells). In this regard, two kinds of miR-21 inhibitors, miR-21 sponge plasmid DNA (Sponge) and anti-miR-21 oligonucleotide (AMO), were transported into MCF-7 cells by PEI-PLL respectively. The miR-21 expression and the cellular physiology were determined post transfection. Compared with the negative control, PEI-PLL/Sponge or PEI-PLL/AMO groups exhibited lower miR-21 expression and cell viability. The anti-tumor mechanism of PEI-PLL/miR-21 inhibitors was further studied by cell cycle and western blot analyses. The results indicated that the miR-21 inhibition could induce the cell cycle arrest in G1 phase, upregulate the expression of Programmed Cell Death Protein 4（PDCD4） and thus active the caspase-3 apoptosis pathway. Interestingly, the PEI-PLL/Sponge and PEI-PLL/AMO also sensitized the MCF-7 cells to anti-tumor drugs, doxorubicin (DOX) and cisplatin (CDDP). These results demonstrated that PEI-PLL/Sponge and PEI-PLL/AMO complexes would be two novel and promising gene delivery systems for breast cancer gene therapy based on miR-21 inhibition.

Keywords： Breast cancer therapy, Polyethylenimine, Polylysine, MiRNA-21 sponge, MiRNA-21 AMO

1. Introduction