Delivery of PRDM 14 siRNA into breast cancer cells via protein-targeted liposomes

From the Clinical Editor

In this study, the authors report a novel approach for targeted intracellular delivery of siRNAs into breast cancer cells through encapsulation into liposomes targeted to the tumor cells with preselected intact phage proteins.[1]

The efficacy of siRNAs as potential anticancer therapeutics can be increased by their targeted delivery into cancer cells via tumor-specific ligands. Phage display offers a unique approach to identify highly specific and selective ligands that can deliver nanocarriers to the site of disease. In this study, we proved a novel approach for intracellular delivery of siRNAs into breast cancer cells through their encapsulation into liposomes targeted to the tumor cells with preselected intact phage proteins. The targeted siRNA liposomes were obtained by a fusion of two parental liposomes containing spontaneously inserted siRNA and fusion phage proteins. The presence of pVIII coat protein fused to a MCF-7 cell-targeting peptide DMPGTVLP in the liposomes was confirmed by Western blotting. The novel phage-targeted siRNA-nanopharmaceuticals demonstrate significant down-regulation of PRDM14 gene expression and PRDM14 protein synthesis in the target MCF-7 cells. This approach offers the potential for development of new anticancer siRNA-based targeted nanomedicines.

Figure 1 shows that PRDM14 siRNA plus DOXO doxorubicin (yellow and red bars) was effective in breast cancer cell killing in DOXO resistant breast cancer cells (first two blue bar at 4-8ng/ml doses). At 32ng/ml of DOXO, PRDM14 siRNA plus DOXO killed 60% of breast cancer cells after one dose compared to only 20% for DOXO alone, showing a 3 fold increase in favor of the combination (data on file at ARIZ Precision Medicine).

1 Bookbinder L, Torchilin VP, Petrenko VA, et. al Nanomedicine. 2011 Jun;7(3):315-23

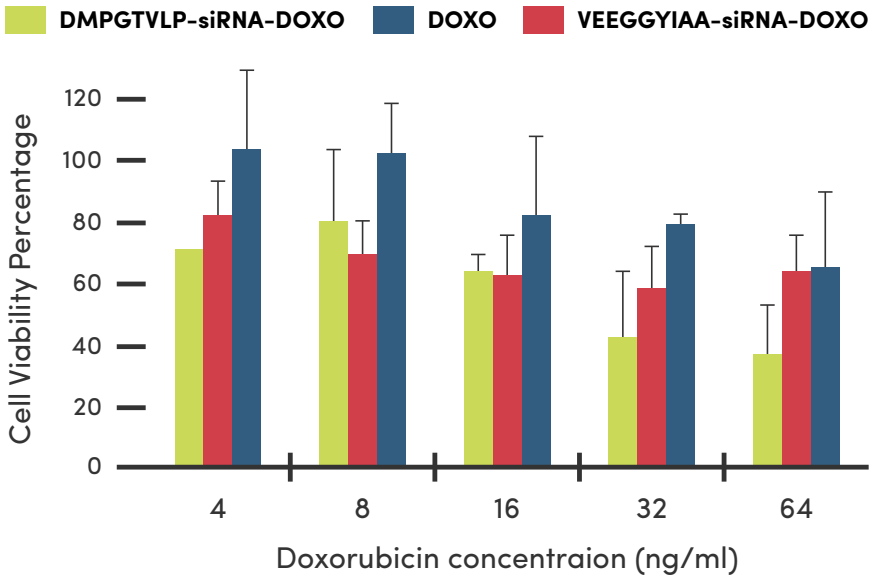

Figure 1 – Cell Viability Percentage

The phage-DMPGTVLP-siRNA-DOXO liposome formation shows a higher cytotoxicity efficiency compared to phage-VEEGGYIAA-siRNA-DOXO for same concentration of protein, siRNA and DOXO. The efficacy becomes much higher when compared to phage-frees/siRNA-free DOXO for same DOXO concentration.

P value for comparison of phage-DMPGTVLP-siRNA-DOXO and phage-free/siRNA-free/DOXO: 0.001, P-value.

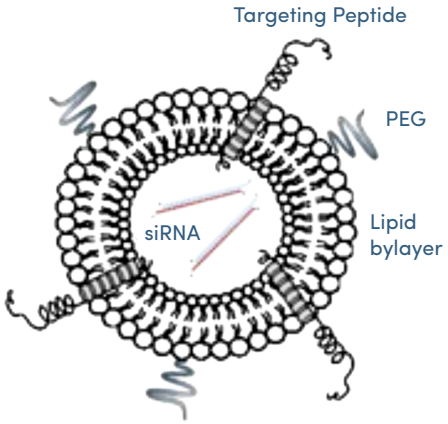

Figure 2

PRDM 14 siRNA-loaded liposome targeted by phage protein fused with a MCF-7 cell-specific peptide DMPGTVLP. The PRDM 14 siRNA molecules are pictured as strands inside the liposomes.

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