# Chitosan Nanoparticles for siRNA Based Gene Silencing Therapy for Cancer

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## Abstract

Small interfering RNA (siRNA) based gene silencing that reduces the synthesis of specific harmful proteins at mRNA level is one of the effective targeted therapies for cancer [1,2]. However, siRNA delivery into the cells is limited due to its rapid decomposition by nucleases and poor cellular uptake [3]. The polycationic, non-toxic, biodegradable and biocompatible polymer such as chitosan (CS) can be bound effectively to siRNA molecule and it can be protected against to enzymatic degradation [4]. In this study CS nanoparticles (NPs) were produced via ionic gelation method and sodium tripolyphosphate (TPP) was used as crosslinker. pH value of the CS solution (4.0 to 5.0) and CS/TPP mass ratio (2.5:1 to 5:1) were changed to optimize the NPs size and surface charge for efficient gene transfection. Morphological characterization of the CS-NPs was evaluated by AFM and SEM. The genes for ABCE1 (ATP-binding casette E1) and eRF3 (eukaryotic release factor 3) proteins which play significant roles in protein synthesis were chosen as target genes to be loaded with CS-NPs, individually and together. Loading efficiencies of 98.69%±0.051 and 98.83%±0.047 were achieved when ABCE1 siRNA and eRF3 siRNA were entrapped into the NPs, respectively. Cellular uptake of fluorescein labeled CS-NPs into MCF-7 cells, WST-1 cytotoxicity and Real Time Cell Analyzer (RTCA) assays of the NPs were carried out. Mean diameter of the CS-NPs was obtained between 105-230 nm and the zeta potential was 27 mV at pH 4.5 and 3:1 CS/TPP mass ratio values. Fig. 1 shows that CS-NPs are spherical in shape by SEM analysis. Both WST-1 and RTCA assays revealed that ABCE1 siRNA, eRF3 siRNA and ABCE1/eRF3 siRNA loaded NPs significantly reduced the cell viabilty and proliferation (Figure 2). This work demonstrated that the CS-NPs suitable in size and surface charge are promising vectors for siRNA based targeted cancer therapy.

## References

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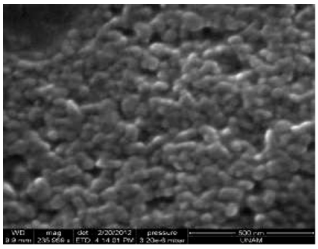

**Figure 1.** SEM micrographs of CS-NPs

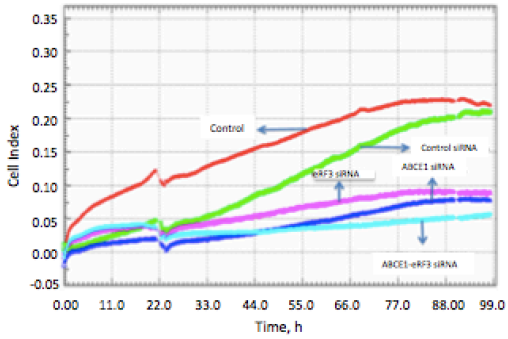


**Figure 2.** Cell proliferation curve of MCF-7 cells treated with control and siRNA loaded CS-NPs