Drug Delivery for Colon Cancer Therapy by Doxorubicin with Oligonucleotide modified Gold-nanoparticles

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Abstract - The major problem associated with chemotherapy is the inability to deliver pharmaceuticals to specific site of the body without inducing normal tissue toxicity. Gold nanoparticles are promising drug delivery systems to overcome multidrug resistance, which is a main cause of ineffective chemotherapy treatment. We designed the nano-complex by nanoparticle and oligonucleotide for drug delivery. We used doxorubicin (DOX) for chemotherapeutic agents, and gold nanoparticle (AuNPs), oligonucleotide (ONTs) complex for drug carrier. The efficacy of cancer treatment with AOD was 2 fold higher than DOX only treatment group. AuNP-ONT-Dox may be a potent new therapeutic agent to increase the efficacy of the drug by overcoming the resistance to doxorubicin in colon cancer cell lines and in vivo nude mouse model.

Keywords: Colon cancer, Doxorubicin, Oligonucleotide, Gold, Nanoparticles

1 Introduction

Methods of colorectal cancer treatment include radical surgery, radiotherapy and chemotherapy. However, the use of chemotherapeutic drugs is limited due to their adverse side-effects, low biodistribution after intravenous administration and multidrug resistance. The major problem associated with chemotherapy is the inability to deliver pharmaceuticals to specific site of the body without inducing normal tissue toxicity. Gold nanoparticles are promising drug delivery systems to overcome multidrug resistance, which is a main cause of ineffective chemotherapy treatment. The aim of this study was to investigate the therapeutic efficacy of gold nanoparticles (AuNPs) containing doxorubicin in in vitro and in vivo colon cancer model.

2 Methods

We designed the nano-complex by nanoparticle and oligonucleotide for drug delivery. We used doxorubicin (DOX) for chemotherapeutic agents, and gold nanoparticle (AuNPs), oligonucleotide (ONTs) complex for drug carrier. A novel colorectal cancer model was established in nude mice. The efficacy of the AOD was tested in vitro experiment using SW 480 colon cancer cell lines. The colon cancer cell proliferation test was done using MTT assay. The therapeutic efficacy of the AuNP-DOX-ONT NPs versus DOX was investigated in tumor bearing nude mouse model.

3 Results

3.1 Characterization of AOD drug Carrier

Figure 1. Characterization of AOD drug carrier with various methods. (a) is TEM image of gold nanoparticles and particle size distribution. (b) is absorption spectrum of each steps of experiments. (c) is fluorescence spectra of doxorubicin standard solution and AOD's supernatant.

3.2 Cell viability-MTT assay

Figure 2. Results of the cell viability assay. Red bar were
control group (treatment with Doxorubicin) and Blue bar were experiment group (treatment with complex of AuNP/e/Doxofubicin)

3.3 Confocal microscopy

Figure 3. Confocal microscopy images of SW 480 cells incubated with AOD

3.4 Tumor proliferation, in vivo

Figure 4. The effect of AOD (AuNP/Oligo/DOXO) on the growth SW480 cells in nude mouse. Tumor volume was monitored over time. The tumor size of AOD treatment group was significantly smaller than only treatment Doxorubicin or PBS group. (p<0.05)

4 Conclusions

The efficacy of cancer treatment with AOD was 2 fold higher than DOX only treatment group. A higher cytotoxic effect of AuNP-ONT-Dox than that of free doxorubicin has been observed in colon cancer cell lines. Intratumoral injection of gold nanoparticles (AuNPs) conjugated to doxorubicin (Au-Dox) is effective against human colon tumors in mice. Au-Dox suppresses growth of colon cancers in tumor bearing nude mice.

AuNP-ONT-Dox may be a potent new therapeutic agent to increase the efficacy of the drug by overcoming the resistance to doxorubicin in colon cancer cell lines and in vivo nude mouse model. Therefore, we strongly believe that gold nanoparticles will be useful for the development of colon cancer therapy using nanomedicine approach.

5 References