Development of a Novel Nanoparticle in Combination with Dual Targeting and Therapeutic Drug Delivery Platform for the Treatment Prostate Cancer

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INTRODUCTION

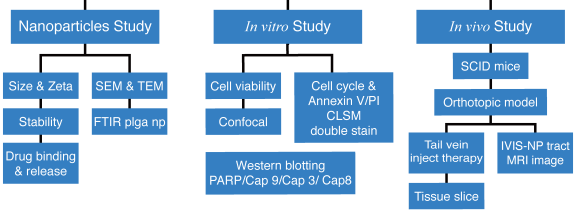
Prostate cancer is the leading cause of cancer death in adult male and multi-stage disease with therapeutic challenges of local recurrent advanced tumors and distant metastatic disease. There is a great increasing interest in designing carrier system with combined therapeutic and diagnostic modalities for proficient delivery of treatment agents to active targeting toward the tumor site. However, the single ligand-based targeting nanocarriers are usually still dissatisfactory as far as selectivity or efficiency are concerned, thus dual-targeted vectors in cancers have been investigated.

We assessed the potential of activated nanoparticle delivery system comprising fucoidan/hyaluronic acid to attain dual-targeted receptor complex with polyethylene glycol-gelatin containing encapsulated epigallocatechin gallate, which could facilitate targeted drug delivery to the prostate tumor and imaging tracking in which position. The study shows successful transfer nanoparticles and internalization into prostate cancer cells through fucose/CD44 ligand recognition and useful to provide drugs, following by inhibition of cell growth via apoptosis-inducing protein.

In the future, the dual-targeted nanoparticles will use to suppress orthotopic prostate tumor activity and accurately target and detect tumor location *in vivo* study.

STUDY & DESIGN METHODS

Application of Dual-target Nanoparticles Loaded EGCG for Prostate Cancer Therapy



RESULTS

Nanoparticles Model

Figure 1.
Design model of the nanoparticel

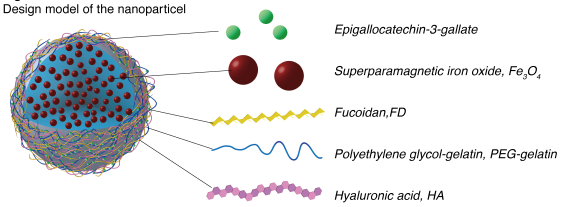


Figure 2.
Fucose/CD44 binding model of the nanoparticel

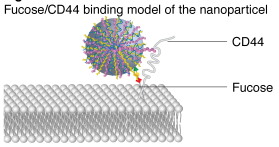
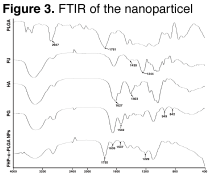


Figure 3. FTIR of the nanoparticel



FU:HA:PG (mg/mL)	Mean Particle Size (nm)	Polydispersity indices	Zeta Potential Value (mV)
0.0:0.0:0.0	158.64 ± 9.87	0.13 ± 0.04	-28.76 ± 2.47
0.6:0.6:0.6	177.57 ± 7.98	0.17 ± 0.06	-30.87 ± 1.78
1.2:1.2:1.2	198.89 ± 12.56	0.22 ± 0.09	-33.75 ± 1.24
2.4:2.4:2.4	252.47 ± 19.76	0.43 ± 0.16	-36.37 ± 3.87

Table 1. Effect of different FU/HA/PG concentrations on particle sizes, polydispersity indices, and zeta potential values of the FHP–c-PLGA NPs (n = 5).

FU/HA/PG concentration at 1.2:1.2:1.2 (mg/mL) (n=5)					
EGCG (mg/mL)	Mean Particle Size (nm)	Polydispersity indices	Zeta Potential Value (mV)	Loading efficiency (%)	Loading content (%)
0.0	198.89 ± 12.56	0.22 ± 0.09	-33.75 ± 1.24	ND	ND
0.5	208.79 ± 8.78	0.24 ± 0.11	-34.89 ± 1.87	43.98 ± 7.87	9.87 ± 1.69
1.0	217.19 ± 11.37	0.25 ± 0.09	-35.75 ± 2.39	47.86 ± 4.57	19.67 ± 2.48
1.5	238.86 ± 13.27	0.29 ± 0.08	-34.97 ± 1.12	37.96 ± 6.68	22.17 ± 3.98

Table 2. Effect of different EGCG concentration on particle sizes, polydispersity indices, zeta potential values, and drug-loading efficiency of EGCG loaded FHP–c-PLGA NPs

FU/HA/PG concentration at 1.2:1.2:1.2 (mg/mL) (n=5)			
PLGA:SPIO (mg/mL)	Mean Particle Size (nm)	Polydispersity indices	Zeta Potential Value (mV)
2.00:0.05	232.64 ± 13.87	0.28 ± 0.04	-36.76 ± 2.47
2.00:0.10	319.57 ± 19.68	0.39 ± 0.12	-38.52 ± 5.91
2.00:0.20	598.90 ± 49.45	0.72 ± 0.27	-37.52 ± 2.35

Table 3. Effect of different PLGA/SPIO concentrations on particle sizes, polydispersity indices, and zeta potential values of the FHP–c-PLGA/PLGA/SPIO NPs

Cell Apoptosis & Western Blotting

Figure 7.
Cell cycle regulation of EGCG-loaded nanoparticle to Luc-PC3.

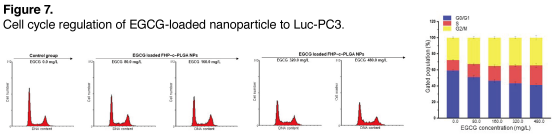
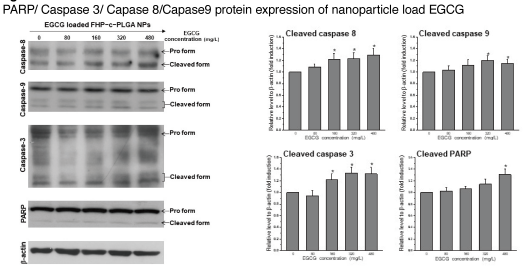
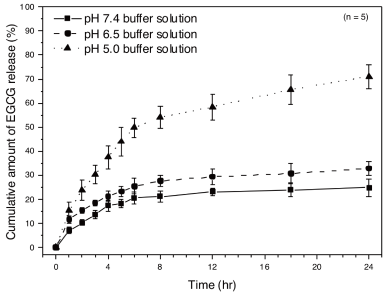


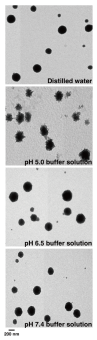
Figure 8.
PARP/ Caspase 3/ Caspase 8/Capase9 protein expression of nanoparticle load EGCG



Drug Releaseing of Nanoparticle

Figure 4.
Drug releasing of nanoparticle in pH 7.4, pH 6.5 and pH 5.0 buffer solution.





In vitro Study

Figure 5.
Cell Viability Comparison of nanoparticle without drug, EGCG-loaded nanoparticle and EGCG solution.

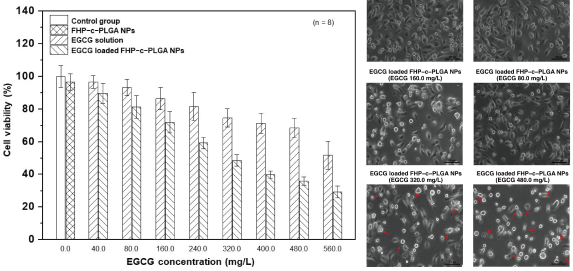
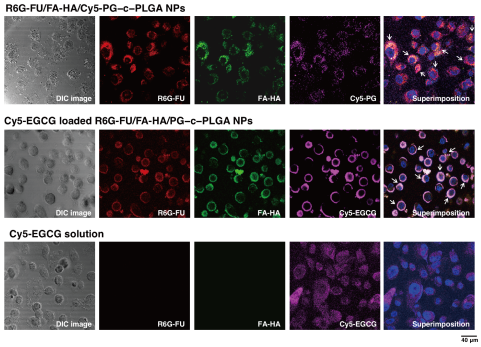


Figure 6.
Confocal images of prostate cancer cells showing the cellular distribution of the NP preparations. Treatment with only R6G-FU/FA-HA/Cy5-PG–c–PLGA NPs or Cy5-EGCG-loaded R6G-FU/FA-HA/PG –c–PLGA NPs vs Cy5-EGCG



CONCLUSION

The present NPs with combined therapeutic and molecular imaging properties can effectively dually target prostate cancers via interactions with the fucose and CD44 receptors, leading to significant enhancement of anti-prostate cancer activity. These multifunctional NPs have the potential to provide a delivery system for identifying alternative anticancer treatment and new diagnostic techniques that will facilitate clinical trials.

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