Photosensitizer encapsulated Hyaluronic Acid Nanoparticles for Photodynamic Therapy of Tumor

Hong Yeol Yoon[1,2], Ki Young Choi[1,2], Heebeom Koo[2], Kwangmeyung Kim[2], Ick Chan Kwon[2], Jae Hyung Park[1,3]

[1] Department of Life and Nanopharmaceutical Sciences, Kyung Hee University, Seoul 130-701, South Korea
[2] Biomedical Research Center, Korea Institute of Science and Technology, Seoul 136-791, Republic of Korea
[3] Department of Chemical Engineering, College of Engineering, Kyung Hee University, Gyeonggi-do 449-701, South Korea

Introduction

In the several years, it has been demonstrated that self-assembled hyaluronic acid (HA) nanoparticles have been efficient active targeting ability to tumor cells via enhanced permieation and retention effect (EPR) and specific binding on receptor such as CD44. [1] Self-assembled HA nanoparticles have shown prolonged circulation in the bloodstream by hydrophilic shell and hydrophobic core effectively encapsulated a quantity of poorly water-soluble anticancer drugs or photosensitizers. [2]

The photosensitizers (PS) used in photodynamic therapy (PDT) transfer energy to molecular oxygen, leading to generation of cytotoxic singlet oxygen or other reactive oxygen species, which irreversible damage to cellular components. [3] However most of PSs have relatively narrow therapeutic windows and are associated with side effects, such as photosensitivity upon exposure to sunlight due to skin accumulation. [4]

In this study, photosensitizer-encapsulated HA nanoparticles were developed for improving the efficacy of the photodynamic therapy (PDT).

Methods

The HA-5β-cholanic acid conjugate was prepared via formation of the amide bond by 1-Ethyl-3- 3-Dimethylaminopropyl Carbodiimide hydrochloride (EDC) N- Hydroxysuccinimide (NHS) reaction [1], and purified by dialysis in the methanol and distilled water for 3days. Chlorin e6 (Ce6), chosen as the model photosensitizer, was encapsulated in the tetrahydrofuran/distilled water corsolvent system, purified by the dialysis to remove unloaded Ce6. In vitro fluorescence images in 96well, 1 ^{4} of MDA-MB231, HT29, SCC7 tumor cell and NIH3T3 normal cell was seeded. Each well treated 100μg/ml Ce6 and after 1hour measured KODAK image station. In vivo biodistribution was measured by Explore Optix system after i.v. injection of 2.5mg/kg Ce6. And therapeutic efficacy of Ce6 was non-invasively evaluated in the live HT29 tumor-bearing mice after i.v. injection of 2.5mg/kg Ce6.

Results

The particle size of Ce6-loaded HA nanoparticles were in the range of 250nm-280nm, depending on the loading amount of Ce6. Ce6 loaded HA nanoparticles showed strong fluorescence intensity in the tumor cell lines. In the HT29 bearing mice, Ce6 loaded HA nanoparticles leading to specific tumor tissue destruction. The results demonstrated that Ce6-loaded HA nanoparticles were selectively accumulated into the tumor tissue in vivo, resulting in effective suppression of the tumor growth.

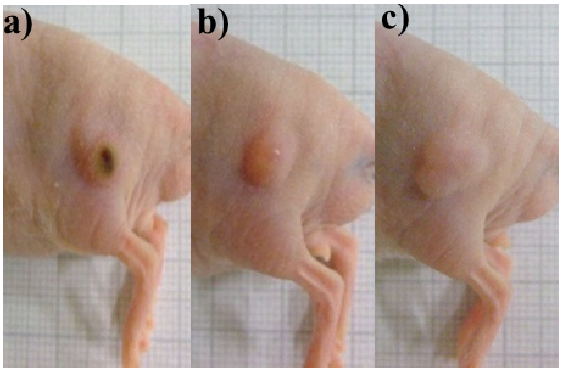

Figure 1. Photodynamic therapy on the HT29 tumor bearing mice; (a) Ce6 encapsulated HA nanoparticles, (b) Ce6, (c) Saline.

Conclusions

Ce6 was successfully encapsulated into the HA nanoparticles. And nanoparticles were stably dispersed in the aqueous condition. Ce6 encapsulated HA nanoparticles specific uptake into the tumor cell line.

HA nanoparticles might have a promising potential as the carrier of photosensitizer for PDT-mediated therapy of various cancers.

References:

1. **Choi, K.Y., et al., Journal of Materials Chemistry, 2009. 19(24): p. 4102-4107.**

2. **Choi, K.Y., et al., Biomaterials, 2010. 31(1): p. 106-14.**

3. **Lee, S.J., et al., Biomaterials, 2009. 30(15): p. 2929-39.**

4. **McCarthy, J.R., et al., Nano Lett, 2005. 5(12): p. 2552-6.**