Efficient *In-Vivo* Photothermal Therapy of Gold Nanorod-Loaded, Functional Nano-Carriers

Won Il Choi[a], Ja-Young Kim[a], Chul Kang[b], Clare C. Byeon[c], Young Ha Kim[a], Giyoong Tae[a,*]
[a]Department of Materials Science and Engineering and Department of Nanobio Materials and Electronics, [b]Nanophotonic Laboratory, Advanced Photonics Research Institute, Gwangju Institute of Science and Technology, Gwangju, Korea.
[c]School of Mechanical Engineering, Kyungpook National University, Daegu, Korea.

Statement of Purpose: Previously, we developed functional Pluronic-based nano-carriers which possessed excellent reservoir characteristics, an effective tumor targeting, long blood circulation time, and low liver uptake [1,2]. In this study, we applied the gold nanorod(GNR)-loaded, Pluronic-based nano-carriers as a hyperthermia agent for enhanced photothermal cancer therapy.

Methods: GNRs (aspect ratio of ~ 4) with a longitudinal absorption band at around 800 nm were synthesized by using a seed-mediated growth method with CTAB-templates. Then, both the bare form and chitosan-conjugated form of Pluronic-based nano-carriers were prepared as carriers for GNRs [2]. The GNRs could be efficiently loaded into the nano-carriers (over 90 %) by using co-incubation at 4 ˚C based on the thermo-sensitive properties of the nano-carriers. The size, zeta potential, morphology, and *in-vitro* stability of the GNR-loaded nano-carriers were characterized. The GNR-loaded nano-carriers were then applied for *in-vitro* photothermal cancer therapy and *in-vivo* solid tumor ablation.

Results: The functional nano-carriers (chitosan-conjugated, Pluronic-based nano-carriers) were prepared by chemically-crosslinking Pluronic F 68 with chitosan conjugation. Instead of applying individual gold nanorods (GNRs), the GNRs were loaded into functional nano-carriers that could provide stable storage of GNRs and selective delivery to a target tumor site. As shown in Figure 1 a), the GNRs were properly loaded inside the nano-carriers for both types without changing the spherical shapes of the nano-carriers. Also, the nano-carriers themselves and the GNR-loaded nano-carriers showed similar average sizes and surface charges, suggesting effective loading of the GNRs inside the nano-carriers (Figure 1 b)). An enhanced *in-vitro* cellular uptake and a photothermal effect were observed for a cancer cell line when the GNR-loaded, chitosan-conjugated nano-carriers were applied than direct application of GNRs. More importantly, an intravenous injection of this system followed by NIR laser irradiation to the tumor site resulted in a very efficient thermolysis *in vivo* (Figure 2 a) and b)). Thus, even apparently complete tumor resorption was achieved without damage to the surrounding tissue, suggesting a promising candidate for clinical phototherapeutic applications (Figure 2 c) and d)).

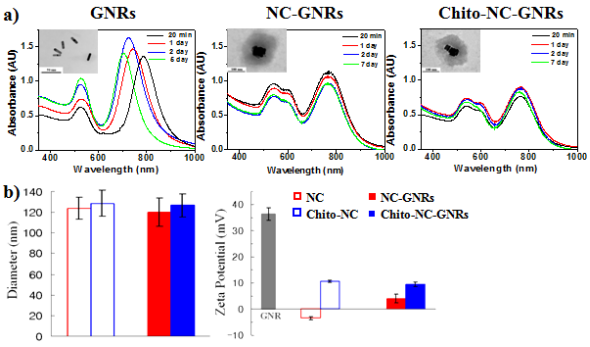

Figure 1. a) Absorption spectra and TEM images (insets), and b) sizes and surface charges of GNRs and GNR-loaded nano-carriers.

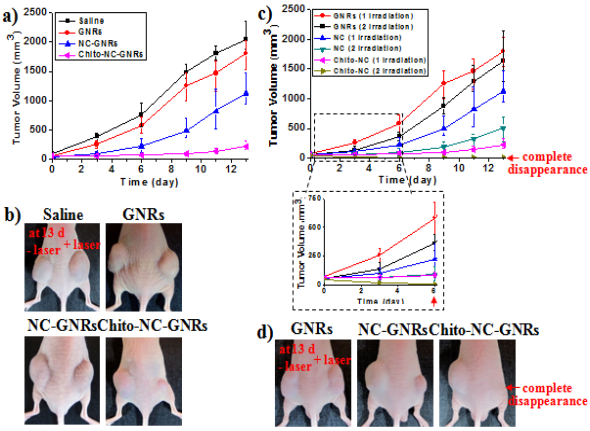

Figure 2. a) Changes in tumor volumes and b) the tumor images after one-time NIR laser irradiation. c) Change in tumor volumes (an enlarged graph at initial time) and d) the tumor images after two-time NIR laser irradiations.

Conclusions: The GNR-loaded, chitosan-conjugated, Pluronic-based nano-carriers could serve as a very effective hyperthermia agent for photothermal cancer therapy with NIR light exposure.

Acknowledgement: Partial financial support by Basic Science Research Program, NRF, MEST, (R15-2008-006-02002-0), and by WCU program at GIST, MEST, Korea (R31-2008-000-10026-0).

References:

[1] Choi, W. I. et al., J Mater Chem. 2008;18:2769-2774.
[2] Kim, J. -Y. et al., J Contol Release. 2010;147:109-117.