Rapid Conversion from Protein-Caged Nanomaterials to Microbubbles: A Sonochemical Route toward Bimodal Imaging Agents

Cheng-An J. Lin,*[†§] Wen-Kai Chuang,[†] Zih-Yun Huang,[†] Shih-Tsung Kang,[+] Ching-Yi Chang,[†] Ching-Ta Chen,[†] Jhih-Liang Li,[†] Jimmy K. Li,[†] Hsueh-Hsiao Wang,[⊥] Fu-Chen Kung,[#] Ji-Lin Shen,[‡§] Wen-Hsiung Chan,[¶§] Chih-Kuang Yeh,[+] Hung-I Yeh,[⊥] Wen-Fu T. Lai,[‖] Walter H. Chang[†§]

[†] Departments of Biomedical Engineering, [‡] Physics, [¶]Bioscience Technology, [§] Center for Nano Bioengineering, and Center for Nano-Technology, Chung Yuan Christian University, Chung-Li 32023, Taiwan; [+] Department of Biomedical Engineering and Environmental Sciences, National Tsing Hua University, Hsinchu 30013, Taiwan; [⊥] Departments of Medical Research and Internal Medicine, Mackay Memorial Hospital, and Department of Medicine, Mackay Medical College, Taipei 10449, Taiwan; [#]Department of Health Developing and Health Marketing, Kainan University, Taoyuan 33857, Taiwan; [‖]Graduate Institute of Clinical Medicine, Graduate Institute of Medical Sciences, and Graduate Institute of Biomaterials, Taipei Medical University, Taipei 110, Taiwan

*** chengan_lin@cycu.edu.tw**

Abstract

We report a facile method for nanoparticle (NP)-coated microbubbles (MBs), which can be used for bimodal ultrasound contrast agent. Based on our previous reported amphiphilic polymer [1], hydrophobic NPs not only can be transferred to aqueous solution, but can offer a universal surface for proteins assembly as core-shell complex of NP/protein corona. The polycarboxylate polymer was used successfully for linking inorganic colloidal NPs of different materials (Au, CdSe/ZnS, Fe_3O_4) to BSA protein corona. A second type of protein-caged nanomaterials, protein-caged gold nanoclusters (AuNCs) can be synthesized by intra-protein "biomineralization" or self-assembly of AuNCs with proteins, thus resulting in high photoluminescence in red to near-infrared emission. Both types of protein-caged nanomaterials can be rapidly converted into MBs by introducing sonochemical route, which promote disulfide crosslinking of cysteine residues between protein-caged nanomaterials and free albumin during acoustic cavitation. Further, the functionalization of MBs can be easily achieved by adjusting the original NP/protein mixture. We also demonstrated different imaging modalities with biocompatible AuNC-coated MBs, used in conjunction with both *in vitro*/ *in vivo* ultrasound and fluorescent imaging, which can held many potential applications in medical diagnostics and therapy [2].

References:

[1] Lin, C.-A. J.; Sperling, R. A.; Li, J. K.; Yang, T. Y.; Li, P. Y.; Zanella, M.; Chang, W. H.; Parak, W. G. J., Design of an amphiphilic polymer for nanoparticle coating and functionalization. SMALL 2008, 4, (3), 334-341.

[2] Lin C. A. J., Chuang W.K., Huang Z.Y., Kang S.T., Chang C.Y., Chen C.T., Li J.L., Li J.K., Wang H.H., Kung F.C., Shen J.L., Chan W.H., Yeh C.K., Yeh H.I., Lai W.F.T., and Chang W.H., Rapid Transformation of Protein-Caged Nanomaterials into Microbubbles As Bimodal Imaging Agents, *ACS Nano*, ASAP, 2012. DOI: 10.1021/nn300768d.

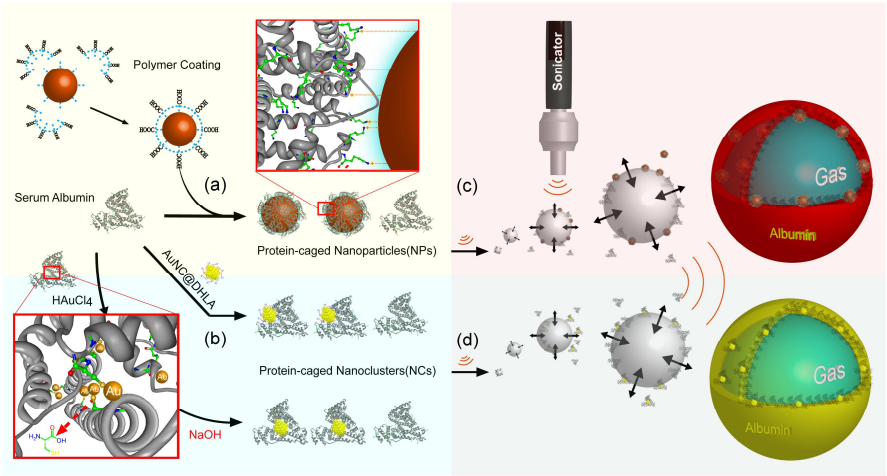

Figure 1. Scheme of synthesis of protein-caged nanomaterials toward dual-functional MBs