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Research review paper

Very small photoluminescent gold nanoparticles for multimodality biomedical imaging☆

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ABSTRACT

An original synthesis method based on X-ray irradiation produced gold nanoparticles (AuNPs) with two important properties for biomedical research: intense visible photoluminescence and very high accumulation in cancer cells. The nanoparticles, coated with MUA (11-mercaptoundecanoid acid), are very small (1.4 nm diameter); the above two properties are not present for even slightly larger sizes. The small MUA-AuNPs are non-cytotoxic (except for very high concentrations) and do not interfere with cancer cell proliferation. Multimodality imaging using visible light fluorescence and X-ray microscopy is demonstrated by tracing the nanoparticle-loaded tumor cells.

Contents

☆ A new type of Au nanoparticles showing strong photoluminescence and high cellular uptake enables in vivo multimodality (X-ray and visible light) imaging and tracing of mouse tumors.

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1. Introduction

The interaction of AuNPs with cells was intensively investigated (Besner et al., 2009; Daniel and Astruc 2004; Ghosh et al., 2008; Giljohann et al., 2010; Jana et al., 2001; Sau et al., 2001; Schwartzberg et al., 2004; Sivaraman et al., 2010; Yang et al., 2008), in particular as far as physical and biological size effects are concerned (Alkilany and Murphy 2010; Connor et al., 2005; Murphy et al., 2008; Ryan et al., 2007; Shah et al., 2011; Wang SG et al., 2008). However, the properties of very small (<2 nm) nanoparticles are still only partially known. There is an apparent conflict between two basic requirements for biomedical applications: photoluminescence (e.g., for cancer cell tracing) and strong cell accumulation. Indeed, Zheng et al., and other authors (Bo et al., 2007; Duan and Nie; 2007; Lin et al., 2009 Zheng et al., 2007) reported photoluminescence from very small AuNPs or nanoclusters. In parallel, few reports (Chithrani et al., 2006; Jiang et al., 2008) argued that larger (15–50 nm) AuNPs produce the strongest cell accumulation effects.

We were able to reconcile these two properties by using MUA capping and an original synthesis method based on X-ray irradiation of the precursor solution. This approach produced very small (1.4 nm) MUA-AuNPs that are photoluminescent and strongly accumulate in

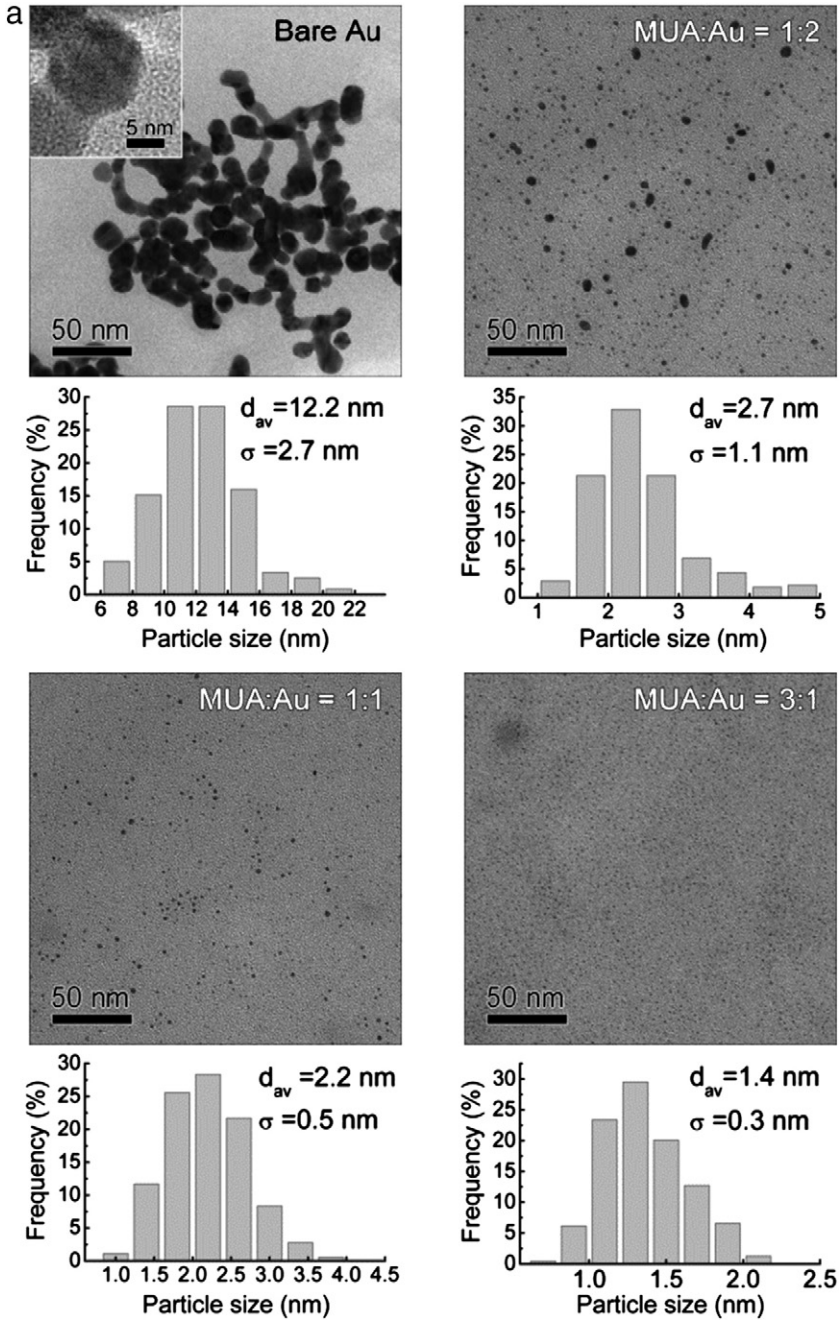

Fig. 1. (a) TEM micrographs with the corresponding size histograms ($n > 200$) and (b) UV–visible spectra of AuNPs synthesized without MUA and with MUA/Au ratios $R = 0.5$, 1 and 3. (c) SAXS scattering profiles of MUA-AuNP colloids with 1 and 0.1 mg ml^{-1} concentration. The 1 mg ml^{-1} profile shows the peaks of interparticle interference at scattering vector magnitudes $q = 0.015$ and 0.034 Å^{-1}, and a hump of the form factor at $q = 0.3$ Å^{-1}. The scattering profile of the 0.1 mg ml^{-1} nanoparticle colloid was fitted using a fuzzy sphere model; the results indicate that the diameter of the nanoparticles plus the MUA coating is ≈3.75 nm.