Chapter 47
Intracellular Behavior of Nanoparticles Based on their Physicochemical Properties

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ABSTRACT

This chapter addresses physicochemical properties that affect Nanoparticle (NP) intracellular behavior using Gold NPs (GNPs) as a model system. The main objective is to outline what is known about the effect of GNP size, shape, and surface properties on cellular uptake and intracellular pathway. The authors propose that the entry of GNPs into cells is related to its effectiveness in applications that favor intracellular localization of such GNPs. The authors also discuss how such properties are used to optimize GNP designs for medical applications. Finally, the authors discuss how GNPs may improve disease diagnosis and treatment. Furthermore, how they may be incorporated or used as alternatives to current treatment options is defined.

INTRODUCTION

Recent advances in engineering and technology have led to the development of many new nanoscale biomedical platforms, including quantum dots, nanoshells, gold nanoparticles, paramagnetic NPs, carbon nanotubes, and improvements in traditional, lipid-based nanoscale platforms. In particular, gold nanoparticles have been explored as a model platform for biomedical research due to their favorable physical and chemical properties (Bergen, van Recum, Goodman, Massey, & Pun, 2006). In this book chapter, spherical colloidal gold nanoparticles are referred to as GNPs while rod-shaped gold nanoparticles are referred to as GNRs. Recent progress in GNP-based research work and understanding how

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physicochemical properties of gold nanoparticles affect intracellular fate will be discussed. Figure 1A is a schematic diagram that highlights some of the important cellular processes involving GNPs that will be discussed in this review. As illustrated, NPs are first internalized by cells through RME and are trapped in organelle called 'endosomes' (Chithrani & Chan, 2007). These endosomes then fuse with lysosomes for processing before being transported to the cell periphery for excretion. These different stages of NP transport through the cell captured by TEM are illustrated in Figure 1B. In the first part of the chapter, current knowledge about physicochemical properties effect on cellular uptake of NPs is discussed. Current understanding of transport properties, organelle distribution, and exocytosis of NPs are also discussed, followed by GNP nuclear targeting and their applications. Finally, the feasibility of incorporating gold nanoparticle into future generations of cancer therapy and imaging applicable NPs, or as multifunctional NPs, will be discussed.

BACKGROUND

GNPs have been receiving significant attention for use in cancer diagnosis and treatment (Brown et al., 2010; Chithrani et al., 2010; El-Sayed, Huang, & El-Sayed, 2006; Huang, El-Sayed, Qian, El-Sayed, 2006; Loo, Lowery, Halas, West, & Drezek, 2005; Wijaya, Schaffer, Pallares, & Hamad-Schifferli, 2009; Zhang et al., 2009; Zheng & Sanche, 2009). There have been a number of studies investigating the potential cytotoxic effects, and intracellular behavior of GNPs as a function of their physicochemical properties (Chithrani & Chan, 2007; Chithrani, Ghazani, & Chan, 2006; Connor, Mwamuka, Gole, Murphy, & Wyatt, 2005; Jiang, Kim, Rutka, & Chan, 2008; Shukla et al., 2005). Most of these investigations have used static methods such as inductively coupled surface plasmon atomic emission spectroscopy, transmission electron microscopy (TEM), and fixed-cell confocal microscopy. However, understanding of the cytoplasmic transport of gold nanostructures in four dimensions (space and time) provides new insight into their intracellular behavior. As initial steps in this direction, surface-enhanced Raman spectroscopy (SERS) and confocal microscopy have been used to probe the interactions of NPs with the cellular environment (Chithrani, Stewart, Allen, & Jaffray, 2009; Huff, Hansen, Zhao, Chen, & Wei, 2007; Kneipp, Kneipp, McLaughlin, Brown, & Kneipp, 2006; Kumar, Harrison, Richards-Kortum, & Sokolov, 2007). Physicochemical properties of NPs including size, shape, surface charge and surface chemistry have been identified as strongly affecting the cellular uptake efficiency. The size and shape of GNPs can be tailored to range between 2-100 nm and their surface properties allow for facile functionalization and targeting to specific biological structures such as the nucleus (Berry, de la Fuente, Mullin, Chu, & Curtis, 2007; Feldherr, Kallenbach, & Schultz, 1984; Jiang et al., 2008; Nativo, Prior, & Brust, 2008; Oyelere, Chen, Huang, El-Sayed, & El-Sayed, 2007; Souza et al., 2006; Tkachenko et al., 2004). In addition, the ability to produce various delivery forms like liposomes, micelles or dendrimers has increased the application scope of GNPs (Carrot et al., 1998; Garcia, Baker, & Crooks, 1999; Mohamed, Ismail, Link, & El-Sayed, 1998; Sung-Hee, Seong-Geun, Ji-Young, & Sung-Sik, 2006). These advantages, along with their biocompatibility, have motivated interest in employing gold nanoparticles in cell imaging, targeted drug and gene delivery, and biosensing (Bergen et al., 2006; Han et al., 2006; Kneipp et al., 2006; Kumar et al., 2007; Sandhu, McIntosh, Simard, Smith, & Rotello, 2002; Shukla et al., 2005; Sokolov et al., 2003).