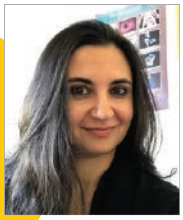
Fluorescent Nanoparticles for Imaging and Diagnostics



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Introduction

In the last decade, fluorescent nanomaterials have demonstrated enormous potential to advance biomedical applications and have provided a deeper understanding of biology and medicine at the molecular level.[1] Fluorescence imaging of cells using either dyes or nanoparticles (NPs) is now among the most widespread methods in biology. Fluorescent NPs sidestep some of the problems inherent to fluorescent dyes based on organic molecules such as low-intensity emission, non-specific binding, and undesired sequestration. In addition, unlike classical dyes, fluorescent NPs guarantee longer *in situ* stability and photostability while maintaining their original optical properties upon interaction with target biomolecules. However, an important limitation of many fluorescent NPs is their cytotoxicity, as in the case of cadmium-based quantum dots. In this regard, the development of silica-based fluorescent nanoparticles shows considerable value. Bright silica nanoparticles have proven to be an excellent material for chemical incorporation and doping with molecular species to enhance their functionality, while guaranteeing long-term biocompatibility. Moreover, because of their unique properties, these NPs have been successfully applied in diagnostics, cancer therapeutics, and gene and drug delivery. The silica NPs offer the following features:

- Ability to adsorb and carry various compounds, such as drugs, oligonucleotides, and proteins
- Low toxicity
- Biodegradability
- Ease of surface functionalization
- Large cellular uptake
- Wide tunability range (from 10 to several hundred nm), while maintaining high monodispersity (Figure 1)
- Ability to incorporate a large number of dye molecules within the silica matrix to yield NPs with varying excitation and emission wavelengths with orders of magnitude higher brightness than organic fluorophores (Figure 2)

The encapsulation of fluorophores within a silica matrix tremendously enhances their chemical stability and prevents photobleaching, which makes them suitable for sensitive biomedical applications.

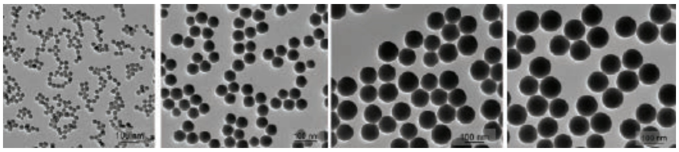

Figure 1. Monodispersed fluorescent silica nanobeads of different sizes. From left to right: 25 nm (**Prod. No. 797901**), 50 nm (**Prod. No. 797952**), 90 nm (**Prod. No. 797944**), and 120 nm (**Prod. No. 797871**).

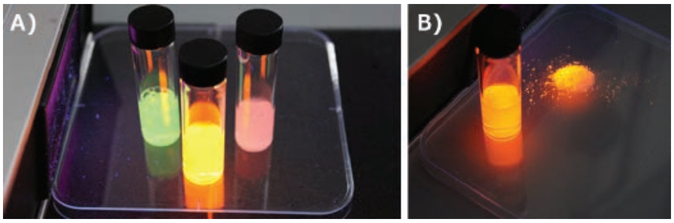

Figure 2. Multicolor fluorescent silica nanobeads dispersed in water and lyophilized form. Emission wavelength of the nanobeads can be tuned from blue to red and infrared.

Bioconjugation and Applications of Fluorescent Silica Nanoparticles

The creation of multifunctional nanoparticles through the integration of optical and chemical properties in a single NP has increased the use of fluorescent NPs in advanced biophysical applications. The presence of a high silanol concentration on the surface of fluorescent silica NPs facilitates a wide variety of surface reactions, including the binding of biomolecules. Several strategies and a variety of surface treatments are available for equipping nanoparticles with the functional groups required for convenient conjugation to biological molecules. Functional groups, such as amines, carboxyls, and thiols can be introduced to the NP surface through the addition of an additional silica coating layer containing the desired functional group. Alkoxysilanes are frequently used as the functionalization molecules; carboxyethylsilanetriol, for example, is used for the introduction of carboxylic acid groups, 3-aminopropyltriethoxysilane for amino groups, and