Lanthanide-Doped Upconverting Nanoparticles: From Synthesis to Applications in Biology

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The recent development of novel highly sensitive and specific luminescent probes with optical properties superior to organic dyes and fluorescent proteins have attracted a diverse group of researchers in a number of key areas. Luminescent nanoparticles such as semiconductor quantum dots (QDs) are emerging as useful tools in diagnostic medicine and therapeutics and are finding widespread applications [1]. However, the majority of these probes require high-energy (UV or blue) light as the excitation source. This has considerable disadvantages resulting in increased background fluorescence (auto-fluorescence), decreased penetration depths in biological tissues as well as photo-induced damage to the specimen under study [2]. To alleviate such issues, multi-photon excited biolabels, including nanoparticles, being more widely used [3]. In particular QDs and gold nanorods (GNRs) are being extensively studied. These nanoparticles are excited with near-infrared (NIR) light, and thus have considerable advantages. For example, NIR light is silent to tissues thus minimizing autofluorescence, possesses greater tissue penetration capabilities and does not cause damage to the sample. Moreover, the nanoparticles require ultrafast (femtosecond) excitation light to induce the multi-photon excited luminescence, which results in increased spatial resolution.

An exciting recent development is the adaption of upconversion for biological applications including biosensing and multi-photon imaging [4-6]. Upconversion is a process inherent to lanthanide-doped materials whereby two (or more) low energy NIR photons are absorbed and in turn, emit higher energy radiation (in the UV-visible-NIR region). This is a very common phenomenon in Ln^{3+}-doped insulating materials because their energy level scheme is favorable for serial addition of multiple isoenergetic photons. Due to the multiphoton nature of the process where “real” long-lived electronic energy states participate, intense upconversion can be observed with low-power commercial cw laser diodes. As a result, inorganic Ln^{3+}-doped nanoparticles are very promising materials and can be used to develop new biocompatible ultra-highly sensitive fluorescent upconverting probes for advanced biomedical applications. Ln^{3+}-doped nanoparticles offer high output, stability with respect to photobleaching, reasonably small size, and flexibility in surface chemistry, which should facilitate their delivery and targeting in biological applications.

Here, we present the synthesis of lanthanide-doped fluoride nanoparticles and subsequent strategies to impart biological functionality. Finally, we show relevant biological applications of these nanoparticles including their ability to be used as imaging probes for malignant cancer cells.

References

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Figures

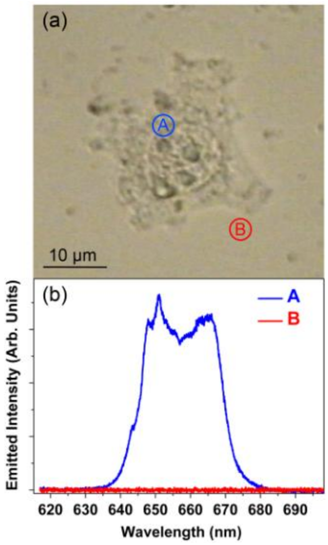

Figure 1: (a) Optical transmission image of a single HeLa cancer cell after 1.5 h incubation in a water solution containing $NaYF_4$:Er^{3+}, Yb^{3+} nanoparticles. (b) Visible two-photon micro-fluorescence spectra obtained when the fs NIR laser is focused inside and outside the HeLa cell (points A and B in the optical transmission image, respectively).

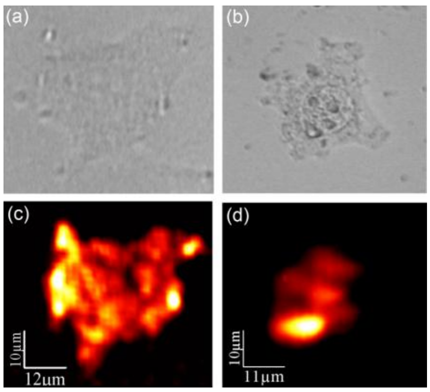

Figure 2: Top – optical transmission images of two HeLa cells after incubation with $NaYF_4$:Er^{3+}, Yb^{3+} nanoparticles during (a) 1.5 and (b) 3 h. Bottom – confocal fluorescence images of the same HeLa cells ((c) and (d) for 1.5 and 3 h incubations, respectively).