Novel nanocrystals with advanced optical properties developed for use as luminescent biomarkers

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Upconversion emission materials are ideal for bioimaging due to its effectiveness as contrast agents for the detection of cancer cells, more so when the background emission of non-cancerous tissues can be minimised. These materials could be used as biomarkers for luminescent labeling of cancerous cells. Opaque tissues can be turned into glassy, transparent substances by using these biomarkers which rely on near-infrared excitation.

The Singapore research team led by Associate Professor Xiaogang Liu and its co-researchers from Saudi Arabia and China succeeded in developing an efficient upconversion process in nanoparticles, ensuring a broad tunability of light emission that could be used in imaging applications. They found a chemical structure that can exhibit efficient upconversion properties through a special arrangement of energy levels. Their synthesis of lanthanide-doped core-shell nanocrystals which resulted in advanced optical properties that can control light, proved to be a novel approach.

For sensing applications, separating optical signals from the background can be tricky when the signal and noise occur at the same wavelength. This problem can be solved with upconversion – a nonlinear optical process – where two low-energy photons of an incident beam can be converted into a single photon of higher energy, which can then be easily distinguished from the background.

The ability to convert light using these nanomaterials for heating also offers promising applications in photodynamic therapy and drug delivery.

The work of Assoc Prof Liu and team was reported in the *Nature Materials* journal, one of the best known materials research-related journals in the world, on 23 October 2011. His team comprises research fellow Dr Feng Wang and graduate students Renren Deng and Juan Wang from the National University of Singapore's (NUS) Department of Chemistry. They worked alongside researchers from King Abdullah University of Science and Technology and Fujian Institute of Research on the Structure of Matter. Assoc Prof Liu and Dr Feng Wang are also scientists at the Institute of Materials Research and Engineering (IMRE), a research institute of Singapore's Agency for Science, Technology and Research (A*STAR).

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A novel approach to cancer detection

The team of researchers focuses on controlling the optical properties of nanomaterials by doping rare-earth metals in confined layer-by-layer structures. The nanoparticle shell can be doped with different rare earth metals, resulting in a broad tunability of the upconverted emission.

By producing nanoparticles with tunable emission which should also have a low toxicity, the researchers have made a great leap in the development of upconverting materials.

Their novel approach involves the designing of core-shell nanoparticles that separates the upconversion process from that of light emission. Photons are absorbed in the core of the nanoparticles and turned into excited electrons, after which they cascade from the core of the nanoparticles into the excited state of rare earth dopants in the shell. While there, these electrons relax and emit light.

Although such sequential energy transfer has been investigated for certain semiconductor nanoparticles and nanowires for solar energy applications, it has not been done so before for rare earth-doped nanoparticles.

Assoc Prof Liu pointed out that effort to find upconverting ions that emit in a wide-ranging spectral region has been unsuccessful until now. This is because an efficient photon upconversion has generally been restricted to a small number of lanthanide ions with emitted light signal detectable by the naked eye.

Explaining his successful approach, Assoc Prof Liu said: "We perform photon upconversion on an array of rare-earth metals. Photon upconversion turns low energy near-infrared light into higher energy made visible with the rational design and chemical synthesis of a core-shell nanostructure."

Assoc Prof Liu and team prepared nanoparticles which could demonstrate an upconversion emission ranging from violet, blue, green to red yellow, with significantly longer infrared excitation wavelengths of up to 980 nm. An important aspect of using light with 980 nm wavelength is such that the transparency of living tissues is high in infrared. This enhances the opportunity for the use of these nanoparticles for cancer detection. Furthermore, the multiple emission colours demonstrated in this research can potentially be used for a more reliable biological diagnostics application, for instance, multiple cell markers.

Opportunities for wider use

The ability to convert low energy near-infrared light into higher energy visible emission, along with low levels of toxicity to cells, and ease of processing, will turn nanometer-sized lanthanide-doped crystals into ideal materials for numerous applications.

According to the group from NUS, the results indicate that a large "library" of luminescent upconversion nanocrystals with distinguishable spectroscopic fingerprints can now be established. When coupled with biological molecules, these nanomaterials would provide a platform for a rapid and reliable route to multiplex detection of cancer or other diseases. The ability of these nanomaterials to induce light-control release of drugs for site-specific delivery also bodes well for future medicine – fewer or reduced side effects can be expected as lanthanide-doped crystals have been tested to be non toxic.

"This work made me confident that we will see exciting new applications for these particles soon," says Thomas Nann, a research professor from the University of South Australia whose research is in this same field. Prof Nann adds that "Up-converting nanoparticles are materials with a tremendous potential for application. However, due to the need for a rigorous selection of usable up-converting ions, Science appeared not to have made any headway for some time prior to this discovery."

Assoc Prof Liu and co-researchers noted the uniqueness of their design, which is the use of core-shell nanostructures and gadolinium ions for energy migration that enhances the ability to produce a wide range of lanthanide-doped nanocrystals to yield upconverted luminescence.

"Benefiting from the sub-lattice of gadolinium ions as a network for energy migration, these judiciously-designed nanoparticles light up those less commonly used lanthanide ions like terbium, europium, and samarium under near-infrared excitation," explains Professor Chun-Hua Yan, a chemistry professor and well known scientist in the same field in

Peking University, China. Adding, Prof Yan says "I do believe that this model, with its uniqueness and versatility, will vastly enrich the currently available upconversion materials, and will have impact on relevant fields such as luminescent biolabelling, multiplexed data storage and display."

The Singapore group has recently filed a related patent for their ground-breaking discovery. Currently, they are working with clinicians to develop clinical diagnostic models for use in a practical manner.

More information: 'Energy migration upconversion in lanthanide-doped core-shell nanocrystals' by Feng Wang, Renren Deng, Juan Wang, Qingxiao Wang, Yu Han, Haomiao Zhu, Xueyuan Chen & Xiaogang Liu was published online on 23 October 2011 in *Nature Materials* (DOI: 10.1038/NMAT3149).

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