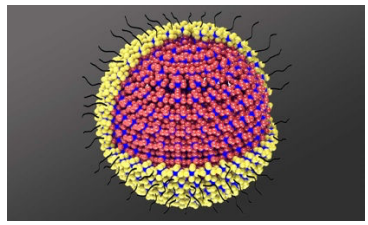

Quantum Dots in Medical Technology
Medical Device Technology
Material Matters, 2006

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During the past few years, the rapidly emerging technology of quantum dots has started to have an impact on the techniques of molecular and cellular imaging in medicine. Their advantages are examined here.

Qdots as materials

Old-fashioned materials scientists, or even metallurgists such as myself may have found it difficult equating some 21st century "materials" with the classical concept that materials were solid substances useful for making objects. The new area of materials chemistry has created some surprising structures that find all sorts of sophisticated applications, and it is important that we address the medical technology opportunities that are presented by these materials advances.

For example, quantum dots allow interesting in vitro and in vivo diagnostic applications. The word quantum implies the smallest piece, and a dot hardly sounds promising for making objects. However, in less than a decade the interest in these objects has grown exponentially and applications, including those in medicine, are rapidly following the establishment of this scientific base. Quantum dots, usually referred to as qdots or QDs, are nanometer- sized crystalline clusters of semiconductors. I have discussed several different aspects of nanotechnology in this column before. Here, we have one significant application of nanomaterials in medicine, in what is now known as nanomedicine, and which is fast becoming recognized as a tremendously important growth area.

The most powerful effects seen with nanomaterials arise when some crucial bulk properties of the parent material are retained and combined with new properties that are only exhibited at nano dimensions; these dimensions can range up to 100 nm, but are usually at the 10 nm level. The two factors that are important here are the much higher surface-to-volume ratio and quantum effects seen at these dimensions. The specific relevant feature of these semiconductor particles is their ability to fluoresce. Consequently, they are becoming a potential alternative in molecular diagnostics because their advantages over conventional fluorescent dyes allow them to be used for tagging viruses and cancer cells.

These advantages include the fact that they have broad excitation spectra (ranging from the ultraviolet to infrared), which can be tuned depending on the size and composition. At the same time, they have narrow emission spectra so that it is possible to resolve the emissions of different qdots in the same sample without much overlap. This is a distinct advantage with complex diagnoses: multicolor labelling with qdots allows identification of the location, distribution and abundance of multiple proteins in, for example, cellular systems. In contrast to some dyes, qdots are highly stable and resistant to degradation, thus, they can be tracked for relatively long times, up to a few hours, in contrast to the seconds or minutes of many dyes, which fade rapidly.

The conjugation of qdots with tissues

If a nanoparticle is going to be useful as a marker for a specific biological structure, it not only has to fluoresce when stimulated so that its presence can be detected and quantified, it also has to attach itself, highly specifically, to the target biomolecule. This is not straightforward because semiconductor materials such as gallium, cadmium and indium compounds are not known for their ability to conjugate to biomolecules at all, let alone with high specificity. Moreover they are usually hydrophobic and incompatible with water-based biological systems. The answers to these problems have been found with surface modification of the semiconductor qdots with organic layers that are able to shield, or exchange with, the hydrophobic groups. These are able to stabilize and solubilize the qdots in the biological environment and provide reactive groups for subsequent conjugation to the appropriate biomolecules. Usually these reactive groups are amine, carboxyl or mercapto groups, and a series of derivatized qdots have been made commercially available with highly specific peptide coatings for targeting small protein domains on cells. Many qdots under investigation for imaging applications are using polyethylene glycol, which has had long use in pharmaceutical products and facilitates conjugation to some target molecules.

Applications of qdots in nanomedicine

So far these qdots have been finding use in fluorescent imaging of biological samples in in vitro diagnostics and investigations, including immunofluorescence assays and live-cell imaging. The way is just now opening up for the in vivo use of qdots. It has to be said that the toxicology of qdot-based products has not been fully addressed, as a recent column in this series on the risks of nanotechnology showed,[1] but animal studies have already revealed the potential here. For example, immunoglobulin G and streptavidin have been coupled to cadmium selenide qdots and used to detect breast cancer cells in animals. It has been shown that it is possible to use a series of delivery techniques to target qdots at tumors, for example, using antibody-conjugated qdots to target a prostate-specific membrane antigen. By combining the considerable photostability of some qdots and using qdots that emit in the near-infrared region (which gives maximal transmission efficiency through tissues), it is also possible to use these techniques in real time to monitor the movement of target cancer cells through tissues and channels.

This subject, as a science, is moving incredibly rapidly and many different opportunities are opening up. It will be surprising if qdots do not find important applications in medical diagnosis and therapy. We trust that the risk analysis of these soon-to-become ubiquitous nanoparticles proceeds at the same pace.

Reference

1. D.F. Williams, "The Risks of Nanotechnology," Medical Device Technology. 16, 9, pp. 6-10 (2005).

Suggested reading

1. M. Bruchez et al., "Semiconductor Nanocrystals as Fluorescent Biological Labels," Science. 281, pp. 2013-2016 (1998).
2. M. Bruchez, "Turning All The Lights On: Quantum Dots In Cellular Assays," Current Opinions in Chem. Biol., 9, pp. 533-5 37 (2005).
3. K.K. Jain, "Nanotechnology In Clinical Laboratory Diagnostics." Clinica Chimica Acta, 358, pp. 37-54 (2005).
4. Y. Wang et al., "Bioapplications of Nanosemiconductors," Materials Today, pp. 20-31 (May 2005).
5. F. Pinaud et al., "Advances In Fluorescence Imaging With Quantum Dot Bio-probes," Biomaterials, 27, pp. 1679-1687 (2006).