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All that Nobel glitters is not biotech gold

Quantum dots won the Nobel Prize, but proved to be a miss in the biomedical space.

This year the Nobel Prize in Chemistry went to three scientists — Moungi Bawendi, Louis Brus and Alexei Ekimov — for the discovery and synthesis of quantum dots. Quantum dots are artificially synthesized nanoscale crystals, usually between 1.5 and 10 nm, that emit various fluorescent colors when exposed to ultraviolet light due to movement of electrons. Larger quantum dots emit longer wavelengths of light, yielding colors like orange or red, while smaller quantum dots emit shorter wavelengths, showing colors such as blue and green.

Today, quantum dots are in television displays and computer monitors, where they provide higher color accuracy and increased brightness as compared with traditional liquid crystal displays. They are also used as fluorescent biological labels to tag specific proteins within a cell or tissue. They make excellent imaging tools because they are extremely bright, have low autofluorescence, show little spectral overlap, and are not as prone to photobleaching as traditional fluorescent markers. Over the last decade or so, quantum dot-based probes have enabled multiplexed cellular imaging that was previously impossible with traditional fluorescent proteins.

In the early 2000s, *Nature Biotechnology* published several papers using quantum dots for in vivo imaging. Kim et al.[1] showed that quantum dots could be used to visualize sentinel lymph nodes in mice and pigs, eliminating the need for a radioactive tracer and a blue dye during surgical procedures. Lidke et al.[2] used fluorescent quantum dots bound to epidermal growth factor (EGF) to investigate how EGF tracks to its receptor. The approach showed that quantum dots attached to natural ligands could serve as effector molecules to provide real-time visualization of signaling mechanisms in cells. Elsewhere, scientists were deploying quantum dots to image capillaries in mouse skin, blood vessels in tumors and the brain extracellular space.

Quantum dots were also showing potential in drug delivery. Here, small-molecule hydrophobic drugs could be embedded between the core and polymer coating or hydrophilic therapeutic agents could be bound to the polymer itself[3–5]. In theory, quantum dots could enable traceable drug delivery, would help in measuring the drug candidates' pharmacodynamics properties and could aid in designing and engineering drug carriers. Quantum dots could be visualized noninvasively and in real time, and would be cheaper than traditional imaging modalities like MRI.

Despite their clinical potential, issues surfaced when using these nanoparticles in vivo. Several papers in the early 2000s showed that quantum dots made with cadmium selenide could kill cells grown in vitro. Cadmium, which is found in most quantum dots because it glows brightly and reliably, is toxic in high doses, although it was not clear how toxic the dots would be in humans. Toxicity depended on the environmental conditions and the quantum dot properties, such as size, charge and concentration[6].

But for human applications, safety has to be paramount, and startups and pharma recognize this. As such, biomedical work with quantum dots stalled in preclinical stages, and the technology moved in a different direction, mostly to the electronics where we find them most today.

Researchers and companies are still trying to make quantum dots work for biomedical applications by generating cadmium-free or nontoxic quantum dots. For example, C-Dots Nanotec creates carbon-based nanodots, avoiding the issues of heavy metals. These nanocrystal 'siblings' to quantum dots can now be used as tags for some of the same applications. But it remains to be seen whether any of these alternatives will gain traction in the biotech space as tools for drug delivery or imaging of cellular processes in vivo, and thus deliver on their original promise for biomedicine.

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