



QUANTUM DOTS: AN OPTIMISTIC APPROACH TO NOVEL THERAPEUTICS

S Mukherjee*, Ushasi Das

NSHM Knowledge Campus, Group of Institutions, Dept. of Pharmacy, B.L Saha Road, Kolkata, India.

*Corresponding author's E-mail: Swarup_mukherjee@rediffmail.com

Accepted on: 15-01-2011; Finalized on: 28-03-2011.

ABSTRACT

Nanotechnology is a multidisciplinary field and has achieved breakthroughs in bioengineering, molecular biology, diagnostics, and therapeutics. Targeted delivery of therapeutic agents has the potential to localize drugs to a specific tissue as a mechanism to enhance treatment efficacy and abrogate side effects. The successful nanoparticle mediated delivery includes the ability to target specific tissues and cell types (primary & secondary targeting) and escape from the uptake by the reticuloendothelial system (RES). The feasibility of *in vivo* targeting of peptides has recently been achieved by using semiconductor quantum dots (Qdots). Qdots are small (<10 nm) inorganic nanocrystals that possess unique luminescent properties; their fluorescence emission is stable and tuned by varying the particle size or composition. It has been found that ZnS-capped CdSe Qdots coated with a lung-targeting peptide accumulate in the lungs of mice after i.v. injection, whereas two other peptides specifically direct Qdots to blood vessels or lymphatic vessels in tumors. Adding polyethylene glycol to the Qdot coating slows down opsonization and prevents nonselective accumulation of Qdots in RES. These results encourage the construction of more complex nanostructures with capabilities such as disease sensing and feedback regulated drug delivery. This work is expected to address the formidable challenges encountered in the field of drug targeting, and opens up new vistas in future development of a promisingly active and site-specific delivery system.

Keywords: Quantum dots, semiconductor, plasmid, fluorophores, liposomes.

INTRODUCTION

A quantum dot is a semiconductor nanostructure that confines the motion of conduction band electrons, valence band holes, or excitons (bound pairs of conduction band electrons and valence band holes) in all three spatial directions. The confinement can be due to electrostatic potentials (generated by external electrodes, doping, strain, impurities), the presence of an interface between different semiconductor materials (e.g. in core-shell nanocrystal systems), the presence of the semiconductor surface (e.g. semiconductor nanocrystal), or a combination of these^{1,2}. A quantum dot has a discrete quantized energy spectrum. The corresponding wave functions are spatially localized within the quantum dot, but extend over many periods of the crystal lattice. A quantum dot contains a small finite number (of the order of 1-100) of conduction band electrons, valence band holes, or excitons, i.e., a finite number of elementary electric charges³⁻⁵. The pubmed search till the date indicates the trends in SLN research, given in fig.1.

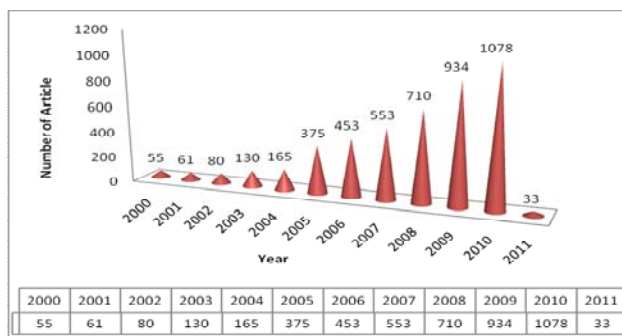


Figure 1: Trends in quantum dots research novel drug delivery

After their discovery, semiconductor quantum dots are emerging as a bona fide industry with a few start-up companies poised to introduce products this year. Initially targeted at biotechnology applications, such as biological reagents and cellular imaging, quantum dots are being eyed by producers for eventual use in light-emitting diodes (LEDs), lasers, and telecommunication devices such as optical amplifiers and waveguides⁶. Sometimes called artificial atoms, quantum dots fall into the category of nanocrystals, which include quantum rods and nanowires. They are technically defined as small semiconductor crystals containing a variable number of electrons that occupy well-defined, discrete quantum states (Fig 2).

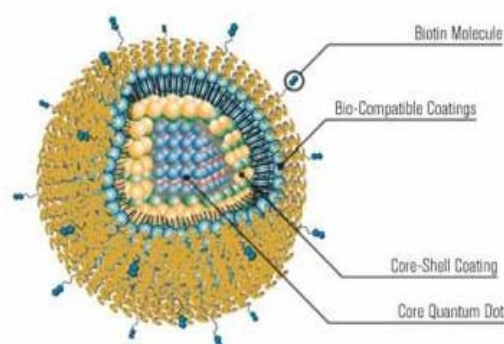


Figure 2: Basic core structure of Q dots

Advantages over Organic Dye-Based Fluorophores⁷

Quantum dot based fluorescent probes are engineered to avoid the many shortcomings of organic dye based fluorophores and they have unique advantages i.e.

Photostability - They have greater photostability than traditional dyes and will still fluoresce after one hour of continuous excitation.

Signal to Noise Ratio - Easily excited using excitation sources hundreds of nanometers away from the emission wavelength, improving the signal to noise ratio in many forms of assays.

Narrow Emission - Very narrow, symmetric emissions enable multiplexing assays.

Brightness - They have bright fluorescence with larger excitation co-efficient at lower wavelengths.

Fluorescent Lifetimes - They are highly photo-resistant with significantly longer fluorescence lifetimes. Researchers can use their intense fluorescence to track individual molecules.

Single excitation source possible - Essentially every quantum dot can be excited by the same source. Just use a shorter wavelength light source (Blue or UV preferable).

Sensitive and precise - Due to their large Stokes Shift and sharp emission spectra, our conjugates have high signal intensity with minimal background interference.

Easily excitable - Their broad excitation spectra allow the use of existing excitation sources, making imaging easier. Quantum dot emission frequency is dependent on the size of the quantum dot. It is available in emissions of 520nm (Adirondack Green), 600nm (Fort Orange), 620nm (Maple Red-Orange) and 680nm. EviFluors exhibit unique fluorescent lifetimes and possess optical and electronic properties to enable exploration of many next generation life science applications.

Advantages of Inorganic Quantum Dots over Organic Fluorophores^{8,9}

Compared to traditional organic fluorophores used for fluorescence labelling in biological experiments, inorganic QDs have wider applications due to their high resistance to photobleaching, which enables visualization of the biological material for a longer time. Fluorophores are highly sensitive to their local environment and can undergo photobleaching, an irreversible photooxidation process which makes them non-fluorescent. This is the main limitation for all studies in which the fluorophores labelled structure has to be observed over extended periods of time. Fluorophores can be optically excited only within a narrow range of wavelengths and fluorescent emission is also restricted to a certain range of wavelengths. Whereas QDs can be excited with a single light source having wavelength shorter than the wavelength of fluorescence. The fluorescence spectra of QDs are narrow, symmetric and have no red tail as observed in fluorophores. Various colors can be observed and distinguished without any spectral overlap. Therefore, multicolor labelling of different structures with QDs of different colors became possible. This multiplexed approach is of great interest in

wide ranging applications such as disease diagnosis and drug delivery.

The field of QDs is of multidisciplinary as persons from different scientific disciplines i.e. chemistry, physics, biology and medicine are working together to harness their potential. Their employment for the detection and treatment of cancer is one such application which is of paramount importance.

PROPERTIES AND APPLICATIONS OF QUANTUM DOTS

The most commonly used QD system is the inner semiconductor core of CdSe coated with the outer shell of ZnS. The ZnS shell is responsible for the chemical and optical stability of the CdSe core. QDs can be made to emit fluorescent light in the ultraviolet to infrared spectrum just by varying their size. The wavelength of fluorescence of the QD depends on its energy gap (i.e. the difference between the excited and the ground state) which is determined by the size of the QD. QDs have narrow spectral line widths, very high levels of brightness, large absorption coefficients across a wide spectral range, high photostability and capability of multiplexed detection. They are very bright and stable even under complex *in vivo* conditions that make them suitable for advanced molecular and cellular imaging, drug delivery and for highly sensitive bioassays and diagnostics¹⁰. Highly sensitive real-time imaging with greater resolution and tracking of single receptor molecules on the surface of living cells have been made possible by QD bioconjugates. In most of the cases, functional QD conjugates for cancer detection are composed of a semiconductor core (CdSe, CdTe); an additional shell such as ZnS in the case of CdSe QDs having a higher band gap than CdSe to increase quantum yield; a water soluble hydrophilic coating; and, functionalized antibodies or other biomolecules complementary to the target cancer markers at the tumor sites.

Effect of Surface Functionalization on the Optical Properties of Quantum Dots

Fundamental studies have revealed that luminescence of QD is very much sensitive to the surface functionalization procedures as the interactions of the molecule with the QD's surface change the surface charges on the QD. But many of the QD based probing applications are based on the change in fluorescence of QD after the interaction of the target analyte molecules with the biomolecules functionalized on the QD surface. It has been well reported that the surface functionalization of QDs improves their solubility. But it could reduce their quantum efficiency as well. This has demonstrated in the case of mercapto acetic acid-treated QDs where the quantum efficiency was reduced drastically. But protein functionalized quantum dots tend to retain their quantum efficiency and offer longer shelf life. They can also be further functionalized with multiple



functional groups without decreasing their quantum efficiency^{11,12}.

APPLICATIONS

Pharmaceutical field

In the pharmaceutical domain, for example, liposomes, polymer based micro and nanoparticles have been subjects of intense research and development during the last three decades. In this scenario metallic particles, which use was already suggested in the first half of the '80, are now experiencing a real renaissance. In the field of diagnosis, magnetic resonance imaging is one of the first and up to now the most developed application of metallic particles. But beside this application, a very new generation of biosensors based on the optical properties of colloidal gold and fluorescent nanocrystals, called quantum dots seems to be ready to be implemented in diagnosis and medical imaging. Concerning therapeutic applications, the potentialities of metal nanoparticles to help fulfilling the need of time and space controlled release of drugs has been intuited for a long time. It should also be used for the detection of active ingredients with fluorescence¹³.

Quantum Dots in Early Diagnosis of Cancer

Early screening of cancer is desirable as most tumors are detectable only when they reach a certain size when they contain millions of cells that may already have metastasized. Currently employed diagnostic techniques such as medical imaging, tissue biopsy and bioanalytical assay of body fluids by enzyme linked immunosorbent assay (ELISA) are insufficiently sensitive and specific to detect most types of early-stage cancers. Moreover, these assays are labour intensive, time consuming, expensive and don't have multiplexing capability. On the other hand, QD based detection is rapid, easy and economical enabling quick point-of-care screening of cancer markers. QDs have got unique properties which make them ideal for detecting tumors. These include intense and stable fluorescence for a longer time; resistance to photobleaching, large molar extinction coefficients, and highly sensitive detection due to their ability to absorb and emit light very efficiently. Due to their large surface area-to-volume ratio, a single QD can be conjugated to various molecules, thus making QDs appealing for employment in designing more complex multifunctional nanostructures. Various types of biomarkers such as proteins, specific DNA or mRNA sequences and circulating tumor cells have been identified for cancer diagnosis from serum samples. Therefore, QD based multiplexed approach for the simultaneous identification of many biomarkers would lead to more effective diagnosis of cancer. QDs have been covalently linked to various biomolecules such as antibodies, peptides, nucleic acids and other ligands for fluorescence probing applications. Some of the applications of QDs in biology along with their

tremendous potential for *in vivo* molecular imaging have already been explored¹⁴.

Removal of Quantum Dots from Living Cells

The clearance of QDs from the living animals and their metabolism demands careful attention and in-depth study before the technology can be used in humans for the diagnosis and treatment of cancer. The only way of clearance of protected QDs from the body is by slow filtration and excretion through the kidney as chemical or enzymatic breakdown is highly unlikely^{2,3}.

In-vivo Imaging with quantum dots

Non-targeted near infrared emitting quantum dot core T2-MP EviTags were tested in tumor bearing mice. Optical image was acquired after intravenous injection of 100pmol of T2-MP EviTags (left) or of physiological buffer as a control (right) into the tail vein of tumor bearing mice. In this preliminary experiment, T2-MP EviTags were shown to be capable of generating a reasonable signal to noise image when compared to the control. Further, the biodistribution pattern as determined from the optical image shows favorable clearance of the non-targeted T2-MP EviTags through the lymphatics, kidneys and bladder. Targeting of Q dots by i.v route is showing in Fig.3.

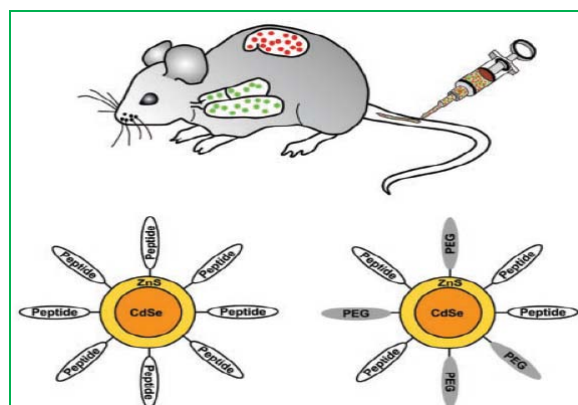


Figure 3: Schematic representation of qdot targeting. Intravenous delivery of Qdots into specific tissues of the mouse. (Upper) Design of peptide-coated Qdots. (Lower) Qdots were coated with either peptide only or with peptides and PEG.. PEG helps the Qdots maintain solubility in aqueous solvents and minimize nonspecific binding.

No uptake in the tumor was observed, suggesting the next round of imaging to be done with tumor targeted T2-MP EviTags will have minimal background signal within the tumor. The development of T2-MP EviTags as non-invasive optical molecular imaging probes will have a great impact on the early detection, diagnosis and treatment monitoring of cancer. The following image demonstrates the ability of InGaP EviTags quantum dots to be imaged *in-vivo* after subcutaneous injection into a mouse liver and tumor⁵.

Self-Illuminating Quantum Dots for in vivo Imaging

Recently, it was demonstrated by Jianghong Rao's group at Stanford University that self-illuminating QD

conjugates (QD-Luc8) have potential applications for *in vivo* imaging. The group developed an eight-mutation variant of *Renilla reniformis* luciferase (Luc8) that is more stable in serum and has improved catalytic efficiency. Luc8 was conjugated to polymer-coated CdSe/ZnS core shell QD 655 for making self-illuminating QD conjugates employing 1-ethyl-3-(3-dimethyl aminopropyl) carbodiimide hydrochloride (EDC) crosslinker. Thus, the QD conjugates formed were self-illuminating as they luminesce by bioluminescence resonance energy transfer (BRET) in the absence of external excitation. BRET is a process in which energy is transferred non-radiatively from a light-emitting donor protein such as *R. reniformis* luciferase to an acceptor fluorescent protein nearby. It resulted in greatly enhanced sensitivity in small animal imaging compared to the existing QDs. One of the greatest advantage of QDs for *in vivo* imaging is that their emission wavelengths can be tuned throughout the near-infrared spectrum by adjusting their size, thus resulting in photostable fluorophores highly stable in biological buffers. This is due to the fact that deep tissue optical imaging is best in near-infrared spectrum as the Rayleigh scattering decreases with increasing wavelength and the major chromophores in animals i.e. hemoglobin and water have local minima in absorption in this spectrum. Antibodies against the cancer biomarkers to be detected were bound to the QD-Luc8 complex using EDC. The resulting QD-Luc8-Antibody complex formed was injected in a cancerous mouse intravenously through the tail vein for the detection of cancer biomarkers. The mouse was then anesthetized and transferred into the light tight chamber. Subsequently, after a few minutes, the substrate for Luc8 i.e. coelenterazine was injected intravenously and the *in vivo* bioluminescent images were taken¹¹.

Immunoassay

An immunoassay readout method based on fluorescent imaging analysis with laser confocal scanning is described. The ZnS-coated CdSe quantum dots (ZnS/CdSe QDs) were linked to a detection antibody. Immunoassay was carried out on a glass chip using a sandwich assay approach, where antibody covalently bound to a glass chip was allowed to capture antigen specially. Afterwards, the detection antibody labeled with QD was allowed to bind selectively to the captured antigen. The fluorescent signals of the sandwich conjugate were detected by a laser confocal scanner. A diode laser was used to excite efficiently the fluorescent signals while bovine serum albumin was used to eliminate nonspecific binding sites. The specificity of the QDs-labeled immunoglobulin G (IgG) was tested by an experiment using goat IgG and human IgG samples. The result was consistent with the binding specificity in a sandwich-type assay¹⁰.

Removal of quantum dots toxicity

The usefulness of quantum dots comes from their peak emission frequency extreme sensitivity - quantum mechanical in nature - to both the dot's size and composition. QDs have been touted as possible replacements for organic dyes in the imaging of biological systems, due to their excellent fluorescent properties, good chemical stability, broad excitation ranges and high photobleaching thresholds. However, the main drawback of QDs is their toxicity and therefore their application is problematic. If this toxicity problem could be addressed, QDs may one day be safely utilized in many areas. For instance, cadmium telluride (CdTe - which is toxic) QD based nanocomposites can be used as fluorescent probes for biological imaging, they can also be utilized to monitor targeted drug delivery and for controlled modification of structural and functional properties of intracellular components. Scientists in Ireland have been using gelatin during the production of CdTe QDs thereby reducing the toxicity of the particles. Their approach could be useful for the development of other nanoparticle composites with low toxicity as well⁹.

Bimodal Molecular Imaging

The synthesis of quantum dots with a water-soluble and paramagnetic micellar coating as a molecular imaging probe for both fluorescence microscopy and MRI. The quantum dots preserve their optical properties and have a very high relaxivity. Targeting ligands can be coupled to these pQDs via maleimide or other functional groups⁸. In this study, the paramagnetic quantum dots were functionalized by conjugating them with cyclic RGD peptides and were successfully targeted to human endothelial cells *in vitro*. We infer that this nanoparticulate bimodal contrast agent may be of great use for the detection of (tumor) angiogenesis.

Plasmid DNA with Semiconductor Quantum Dots¹³

Semiconductor nanocrystal quantum dots (QDs) allow long-term imaging in the cellular environment with high photostability. QD bio-labeling techniques have previously been developed for tagging proteins and peptides as well as oligonucleotides. In this contribution, QD-decorated plasmid DNA was utilized for the first time for long-term intracellular and intranuclear tracking studies. Conjugation of plasmid DNA with phospholipid-coated QDs was accomplished using a peptide nucleic acid (PNA) #8211; *N*-succinimidyl-3-(2-pyridylthio) propionate linker. Gel electrophoresis and confocal and atomic force microscopy (AFM) were used to confirm the structure of QD#8211; DNA conjugates. AFM imaging also revealed that multiple QDs were attached in a cluster at the PNA-reactive site of the plasmid DNA. These QD#8211; DNA conjugates were capable of expressing the reporter protein, enhanced green fluorescent protein, following transfection in Chinese hamster ovary (CHO-K1) cells with an efficiency of ca. 62%, which was comparable to the control (unconjugated) plasmid DNA. Quantum dots offer many



technical advantages over traditional fluorescent dyes and newer DNA chip technologies, which are commonly used to detect and track biological molecules. They are brighter and easier to visualize than organic dyes. They are also more flexible and yield faster results than other current technologies, such as DNA chips. In addition to their usefulness in identifying and tracking molecules in basic biomedical studies, quantum dots promise faster, more flexible, and less costly tests for on-the-spot clinical analyses such as screening for illegal drugs and diagnosing conditions ranging from HIV infection to allergies.

Quantum dots for Brain tumor diagnosis¹⁴

The intra-operative diagnosis of brain tumors and the timely evaluation of biomarkers that can guide therapy are hindered by the paucity of rapid adjunctive studies. This study evaluates the feasibility and specificity of using quantum dot-labeled antibodies for rapid visualization of epidermal growth factor receptor (EGFR) expression in human brain tumor cells and in surgical frozen section slides of glioma tissue. Streptavidin-coated quantum dots (QDs) were conjugated to anti-EGFR antibodies and incubated with target cultured tumor cells and tissues. The experiments were conducted first in human glioma tumor cell lines with elevated levels of EGFR expression (SKMG-3, U87) and then in frozen tissue sections of glioblastoma multiforme and of oligodendroglioma. The bioconjugated QDs used in the study were found to bind selectively to brain tumor cells expressing EGFR. QD complexed quickly to the cell membrane (less than 15min), and binding was highly specific and depended on the expression level of EGFR on the cell membrane. Tissue experiments showed that only tumor specimens expressing EGFR were labeled in less than 30min by QD complexes. These findings demonstrate that QD-labeled antibodies can provide a quick and accurate method for characterizing the presence or absence of a specific predictive biomarker¹⁵.

The multiphoton microscopy techniques and transgenic mice that expressed green fluorescent protein, and combined them with the use of quantum dot preparations which shows fluorescent semiconductor nanocrystals can be customized to concurrently image and differentiate tumor vessels from both the perivascular cells and the matrix. Moreover, it used to measure the ability of particles of different sizes to access the tumor and it has successfully monitored the recruitment of quantum dot #8722; labeled bone marrow #8722; derived precursor cells to the tumor vasculature. These examples show the versatility of quantum dots for studying tumor.

Quantum Dots Able to identify Live Breast Cancer Cells¹⁶

A research team from Quantum Dot Corporation and Genentech proved the potential of QDs to identify live breast cancer cells that are likely to respond to an anti-cancer drug. They employed QDs linked to immunoglobulin G (IgG) and Streptavidin to label Her2

cancer marker present on the surface of live breast cancer cells and also explored the QD technology for the simultaneous labelling of Her2 on the cell surface and in the nucleus. The researchers simultaneously detected two cellular targets with a single excitation wavelength thereby showing that different colored QDs i.e. QDs of different sizes but same materials could be used together to distinguish different parts of a single cell thus leading to multiplex target detection.

Biosensor and biolabels¹⁷:

A number of analytical tools have been developed with application of this smart and potential technology. These tools are employed for determination of various pathological proteins and physiological-biochemical indicator associated with disease or disrupted metabolic conditions of body. Various nanoenabled technologies, techniques and their analytical applications are listed below:

Table 1: Nanoenabled technologies, techniques and their analytical applications

Technology	Technique	Application
Bioarrays and Biosensors	Nanofabrication	Nano-Objects Detection
DNA Chips	Lab on Chip Nanotubes	Electrochemical Detection
Protein-Chips	Pill on Chip Nanowires	Optical Detection
Glyco-Chips	Nanofluidics Nanoparticles	Mechanical Detection
Cell-Chips	Nanostructured Surfaces	Electrical Detection

A **biosensor** is generally defined as a measurement system that consists of a probe with a sensitive biological recognition element, or bioreceptor, a physicochemical detector component, and a transducer in between to amplify and transduce these signals in to measurable form. A nanobiosensor or nanosensor is a **biosensor** that has dimensions on the nanometre size scale. Applications of various nanosystems as biosensor and biolabels are given below:

Table 2: Applications of various nanosystems as biosensor and biolabels

Nanosystem	Applications
Gold Nanoparticles	For ssDNA detection; in immunohistochemistry to identify protein-protein interaction
Iron oxide nanocrystal	Monitor gene expression; detect the pathogens such as cancer, brain inflammation, arthritis and atherosclerosis
Nanopores	Sensing single DNA molecules by nanopores
Cantilever array	Diagnosis of diabetes mellitus, for detection of bacteria, fungi, viruses; for cancer diagnosis
Carbon nanotube	Blood glucose monitoring; sensors for DNA detection
Nanowire	Electrical detection of single viruses and biomolecules
Nanoparticle-based biodetection	Detection of pathogenic biomarkers, Ultra-sensitive detection of single bacteria



CONCLUSION

Exactly where quantum dots will find their biggest commercial breakthrough remains to be seen, but the initial applications will surely pave the way for others. Still there is need of more attention should be drawn towards the implementation by researchers and other field. Furthermore, how these tracking devices can be entirely disposed of by the body after achieving their purpose and their minimum side effect should also be measured.

FUTURE APPLICATIONS

Researchers have started the exploration of QDs just from the last two decades. The field is still in its infancy but it has captivated scientists and engineers due to the unique optical and electronic properties of QDs. QDs have revolutionized the field of molecular imaging. The forthcoming years would see their potential applications in different fields. One of the major areas of impact is surely the intracellular imaging of live cells. The technology will provide new insights in understanding the pathophysiology of cancer, and in imaging and screening tumors. QDs will definitely be one of the components of the envisioned multifunctional nanodevices that can detect diseased tissue, provide treatment and report progress in real time.

Anti-counterfeiting capabilities: inject dots into liquid mixtures, fabrics, polymers matrices, etc. Ability to specifically control absorption and emission spectra to produce unique validation signatures. Almost impossible to mimic with traditional semi-conductors.

Counter-espionage/ Defence applications: Integrate quantum dots into dust that tracks enemies. Protection against friendly-fire events.

REFERENCES

1. Maria E. Akerman, Warren C. W. Chan, Pirjo Laakkonen, Sangeeta N. Bhatia, and Erkki Ruoslahti, (2002), *PNAS*. 99, 20:12617–12621.
2. Hakkarainen T, Schramm A, Tukiainen A, Ahorinta R, Toikkanen L, Guina M. "Lateral Ordering of InAs Quantum Dots on Cross-hatch Patterned GaInP." *Nanoscale Res Lett*. 2010 Aug 20; 5(12):1892-1896.
3. Alonso-González P, González L, Martín-Sánchez J, González Y, Fuster D, Sales DL, Hernández-Maldonado D, Herrera M, Molina SI. "Growth of Low-Density Vertical Quantum Dot Molecules with Control in Energy Emission." *Nanoscale Res Lett*. 2010 Sep 5; 5(12):1913-1916.
4. Selvan ST. "Silica-coated quantum dots and magnetic nanoparticles for bioimaging applications" *Biointerphases*. 2010 Sep; 5(3):FA110.
5. Maestro LM, Rodriguez EM, Vetrone F, Naccache R, Ramirez HL, Jaque D, Capobianco JA, Solé JG. "Nanoparticles for highly efficient multiphoton fluorescence bioimaging" *Opt Express*. 2010 Nov 8; 18(23):23544-53. doi: 10.1364/OE.18.023544.
6. Van Manen HJ, Otto C. "Hybrid Raman-fluorescence microscopy on single cells using quantum dots." *Methods Mol Biol*. 2011; 680:45-60.
7. Wang GL, Dong YM, Yang HX, Li ZJ. "Ultrasensitive cysteine sensing using citrate-capped CdS quantum dots" *Talanta*. 2011 Jan 15; 83(3):943-7. Epub 2010 Nov 4.
8. Wang X, Ma XL, Feng X, Zheng YF. "Controlled synthesis and characterization of ZnSe quantum dots." *J Nanosci Nanotechnol*. 2010 Nov; 10(11):7812-5.
9. Xu X, Liu X, Nie Z, Pan Y, Guo M, Yao S. "Label-free fluorescent detection of protein kinase activity based on the aggregation behavior of unmodified quantum dots." *Anal Chem*. 2011 Jan 1; 83(1):52-9. Epub 2010 Dec 3.
10. Yan Y, Wang S, Liu Z, Wang H, Huang D. "CdSe-ZnS quantum dots for selective and sensitive detection and quantification of hypochlorite." *Anal Chem*. 2010 Dec 1; 82(23):9775-81. Epub 2010 Nov 5.
11. Yang K, Cao YA, Shi C, Li ZG, Zhang FJ, Yang J, Zhao C. "Quantum dot-based visual in vivo imaging for oral squamous cell carcinoma in mice." *Oral Oncol*. 2010 Dec; 46(12):864-8. Epub 2010 Nov 3.
12. Cros-Gagneux A, Delpech F, Nayral C, Cornejo A, Coppel Y, Chaudret B. "Surface Chemistry of InP Quantum Dots: A Comprehensive Study." *J Am Chem Soc*. 2010 Dec 29; 132(51):18147-18157. Epub 2010 Dec 2.
13. Di D, Perez-Wurfl I, Gentle A, Kim DH, Hao X, Shi L, Conibeer G, Green MA. "Impacts of Post-metallisation Processes on the Electrical and Photovoltaic Properties of Si Quantum Dot Solar Cells." *Nanoscale Res Lett*. 2010 Aug 1; 5(11):1762-1767.
14. Buranda T, Wu Y, Sklar LA. "Quantum dots for quantitative flow cytometry." *Methods Mol Biol*. 2011; 699:67-84.
15. Huang YX, Zheng XJ, Kang LL, Chen XY, Liu WJ, Huang BT, Wu ZJ. "Quantum dots as a sensor for quantitative visualization of surface charges on single living cells with nano-scale resolution." *Biosens Bioelectron*. 2010 Sep 16.
16. Lee YJ, Lee CJ, Cheng CM. "Enhancing the conversion efficiency of red emission by spin-coating CdSe quantum dots on the green nanorod light-emitting diode." *Opt Express*. 2010 Nov 8; 18 Suppl 4:A554-61. doi: 10.1364/OE.18.00A554.
17. Zhao Y, Zhao L, Zhou L, Zhi Y, Xu J, Wei Z, Zhang KX, Ouellette BF, Shen H. "Quantum dot conjugates for targeted silencing of bcr/abl gene by RNA interference in human myelogenous leukemia K562 cells." *J Nanosci Nanotechnol*. 2010 Aug; 10(8):5137-43.

About Corresponding Author: SWARUPANANDA MUKHERJEE (M.PHARM, MBA, IPR, DPQCQAM (PhD))



Had his post graduation from Rajiv Gandhi University of Health sciences in Bangalore. He has also completed his IPR from Indian Institute of Science, Bangalore and MBA from National Institute of Business Management, Chennai. Recently he is working in NSHM College of Pharmaceutical Technology, Kolkata as an Assistant Professor and as a Research Scholar. He is involved in the research work of nanoparticulate drug delivery system.

