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Invited Review

Medically translatable quantum dots for biosensing and imaging

Youngrong Park[a,1], Sanghwa Jeong[a,1], Sungjee Kim[a,b,*]

[a] Department of Chemistry, Pohang University of Science and Technology (POSTECH), San 31, Hyojadong, Nam-gu, Pohang, 37673, Republic of Korea
[b] School of Interdisciplinary Bioscience and Bioengineering, Pohang University of Science and Technology (POSTECH), San 31, Hyojadong, Nam-gu, Pohang, 37673, Republic of Korea

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ABSTRACT

Photoluminescent quantum dots (QDs) promise many biomedical applications as a new class of optical probes showing unique optical properties such as high brightness, stability, and multiplexing ability. In this review, we focus on recent research interest of medically-translatable QDs for in vitro biomedical sensing and in vivo imaging. QD-based biomedical sensing shows higher selectivity and sensitivity over conventional methods for immunohistochemistry, immunoassay, and enzymatic assays. In addition, QD-based biosensors afford simple detections of multiple biomarkers. QD probes in the second near-infrared region ($1000 \leq \lambda \leq 1700$ nm) show the great potential for in vivo fluorescence imaging because of the suppressed light scattering and the capability for deep tissue penetration. The second near-infrared emitting QDs covered in this review include Ag_2S, Ag_2Se, Ag_2Te, PbS, PbSe, InAs, Cd_3P_2, Cd_6P_7, and Cd_3As_2 QDs. In vivo imaging properties of these QDs are highlighted with special reference to vasculature imaging and tumor localization.

Contents

* Corresponding author at: Department of chemistry and School of Interdisciplinary Bioscience and Bioengineering, Pohang University of Science and Technology (POSTECH), San 31, Hyojadong, Nam-gu, Pohang, 37673, Republic of Korea.
E-mail address: sungjee@postech.ac.kr (S. Kim).
[1] These authors contributed equally.

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Youngrong Park graduated with a Bachelor of Chemistry from Inha University in 2010 and a Ph.D. in Chemistry from Pohang University of Science and Technology (POSTECH) in 2016. Her research activities involve synthesis of inorganic nanoparticles, nanoparticle-biomolecular conjugation, and development of cancer microenvironment sensitive fluorescent probes for cancer diagnosis.

Sanghwa Jeong obtained his undergraduate (2009) and PhD degrees (2015) in Chemistry from Pohang University of Science and Technology (POSTECH). His current research is focused on the synthesis of inorganic nanoparticles and self-assemblies such as semiconductor quantum dots, lanthanide-doped nanoparticles, and carbon nanostructures and the fabrication of near-infrared photoluminescent nanostructures and their applications for bioimaging.

Sungjee Kim is an associate professor in the Department of Chemistry, Pohang University of Science and Technology (POSTECH). His major research interest lies in light–matter interactions at the nanoscale with three overlapped foci of nanophotonics, nanoplasmonics, and nanobiotechnology. He is actively interested in applying quantum dots and other semiconductor nanostructures for biomedical application. See http://nanotrio.com for further details.

1. Introduction

Quantum dots (QDs) are photoluminescent semiconductor nanocrystals that are composed of a few hundred to a few thousand atoms [1,2]. The nanometer size of QDs is small enough to introduce quantum confinement, so they have novel optical and electronic properties that cannot be observed in the bulk semiconductor. The optical properties of QDs can be controlled by adjusting their material composition, size, shape, and surface chemistry. QDs have high quantum yield (QY), photo-stability, broad absorption with large one-photon and two-photon absorption cross-sections, narrow and symmetric photoluminescence from UV to near-infrared (NIR) range, and large effective Stokes shift, which make them excellent fluorescent probes in biomedical applications [3–5]. QDs have a broad absorption spectrum and narrow emission profile that allow simultaneous excitation of multiple fluorescence colors and effective spectral deconvolution of individual photoluminescence signals, and are therefore suitable for multiplexing; simultaneous detection of multiple signals. These advantages of QDs suggest applications of QD-based biosensors for disease diagnosis which are expected to improve the sensitivity and accuracy [6–8]. QDs can be also used as fluorescent probes for in vivo molecular imaging in the second near-infrared (NIR-II; wavelength $1000 \leq \lambda \leq 1700$ nm) region which is a useful range in biomedical applications for disease diagnosis [9,10]. Fluorescence molecular imaging can provide real-time visualization, multiplexing ability, high sensitivity, and noninvasive diagnostic method. Compared to other spectral ranges, NIR-II light is less scattered and absorbed by biomolecules, and therefore penetrates more deeply into tissues, provides improved spatial resolution, and lowers autofluorescence [11,12]. Advancement of NIR-II-fluorescence imaging technology requires development of NIR-II-fluorophores with high quantum yield. QDs are the leading candidate for NIR-II in vivo imaging for biomedical applications. Herein, we showcase recent studies regarding (1) in vitro biomedical applications of QDs for sensing and (2) NIR-II-emitting QDs for in vivo medical imaging through deep tissues. For QD probes to be translated to clinical use, they must have minimal toxicity. Toxicity is less concerned when QD probes are used in vitro application because QD probes used for excised tissues or corrected blood sample from the patient, so this is likely to be one of the most widely-applied clinical applications in the near future. QDs for NIR-II-fluorescent probes are expected to be used for in vivo molecular imaging at the preclinical level and clinical level in the future.

1.1. Synthesis of QDs

Medical applications require brightly-emitting QDs of uniform size and high crystallinity with fewer defects. Semiconductor QDs have been prepared by various methods such as molecular beam epitaxy, solvothermal synthesis in organic solvent with high boiling point, sol-gel processing, and microwave irradiation [13,14]. In the colloidal synthesis of QDs, high reaction temperature has been usually preferred to afford facile rearrangement and annealing of atoms in a QD, which results in bright QDs with suppressed crystal defects. Solvothermal syntheses of colloidal QDs in high boiling point organic solvents such as octadecene and trioctylphosphine have yielded high-quality QDs (Fig. 1) [15,16]. In common solvothermal methods, activated organometalic precursors (e.g., cadmium oleate) in hot solvent are rapidly mixed with chalcogen precursors (e.g., trioctylphosphine selenide), then nucleation and growth proceed to produce QDs. The size and band-gap of QDs can be easily controlled by adjusting the reaction time, temperature, precursor concentration, and amount of surfactant. Various kinds of semiconductor QDs can be produced by choosing appropriate organometallic and anion precursors: examples include CdSe (II–IV group), InP (III–V group), Ag_2Se (I–VI), and $CuInS_2$ (I–III–VI group).

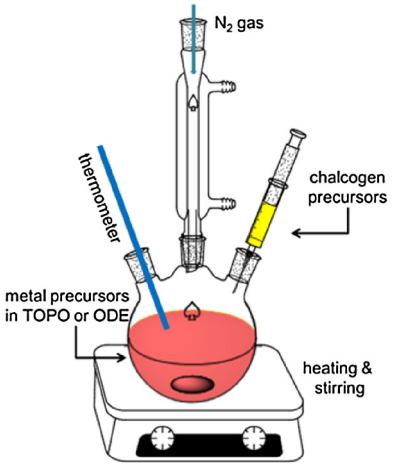

Fig. 1. Schematic illustration of the solvothermal synthesis of colloidal QDs.