## Novel compact water soluble quantum dots and their structural characterization using time-resolved Förster resonance energy transfer.

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The superior advantages of semiconductor nanocrystal (QDs) were demonstrated in numerous applications in nanobiotechnology <sup>1</sup>. The majority of the QD syntheses are performed in organic solution, which makes the phase transfer to an important step for their further utilization. Thereby the surface manipulation has an influence on the photophysical parameters, such as the photoluminescence maximum and quantum yield. The maintaining of those values after the phase transfer are of importance for further application. Additionally the manipulation also contribute to the overall size of the QD, which is a critical parameter in biological application.

Especially Förster resonance energy transfer (FRET), which is an important signal transduction pathway for biological recognition events, show a high distance sensitivity. FRET is non-radiative energy transfer from a donor to an acceptor based on Coulomb interaction. Despite of the utilization of QDs as FRET donors, they also can be used as acceptors in combination with lanthanide terbium complexes (LTCs). This combination is able to outperform classical antibody based sandwich immunoassays for the detection and quantification of cancer markers in serum samples in terms of sensitivity and multiplexed application <sup>2</sup>. Another promising advantage of FRET is the utilization as spectroscopic ruler for the structural analysis in the nanometer range. Especially the characterization of QDs in the aqueous phase is difficult. Common structural analysis methods, such as transmission electron microscopy (TEM) or dynamic light scattering (DLS), have limitations in terms of homogenous measurements and the inclusion of a hydration shell.

In this contribution we will present a novel approach to render in house and commercial QDs water soluble, which enabled the preparation of the smallest antibody-functionalized QD probe ever reported. Furthermore, we will demonstrate the advantages of this preparation by comparison to commercial QDs for the quantification of the prostate cancer marker inside homogenous FRET immunoassays with LTCs as donors <sup>3</sup>. Additionally we will demonstrate the utilization of time-resolved analysis of the decay times of LTC-QD FRET systems for the structural analysis of QDs. This approach allows for the first time the simultaneous estimation of size and shape at the same concentration (nanomolar) and in the same biological environment as used for the biological application. A detailed time-resolved study of 11 QDs with different sizes, shapes and surface coatings will confirm the large potential of the new nano-tool for the structural analysis of QDs <sup>4</sup>.

<sup>1.</sup> Wegner, K.D. et al., Quantum dots: Bright and versatile In vitro and In vivo Fluorescence Imaging Biosensors, Chem. Soc. Rev. 44, 4792-4834, 2015

Wegner, K.D. et al., Quantum-Dot-Based Förster Resonance Energy Transfer Immunoassay for Sensitive Clinical Diagnostics of Low-Volume Serum Samples, ACS Nano 7(8), 7411-7419, 2013

<sup>3.</sup> Materra, L. et al., Compact quantum dot-antibody conjugates for FRET immunoassays with subnanomolar detection limits, Nanoscale, DOI :10.1039/C6NR03261C, 2016

Wegner, K.D. et al., Three-Dimensional Solution-Phase Förster Resonance Energy Transfer Analysis of Nanomolar Quantum Dot Bioconjugates with Subnanometer Resolution, Chem. Mater. 26 (14), 4299-4312, 2014