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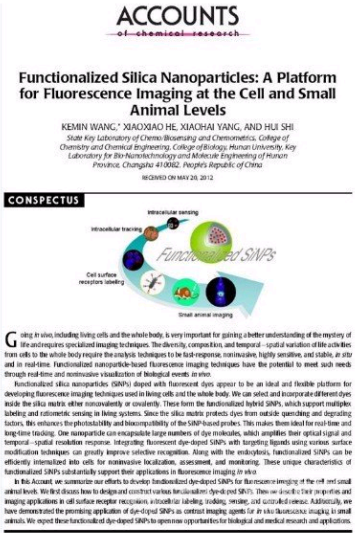
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Functionalized Silica Nanoparticles: A Platform for Fluorescence Imaging at the Cell and Small Animal Levels

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CONSPECTUS

Intracellular sensing
Intracellular tracking
Functionalized SiNPs
Cell surface receptors labeling
Small animal imaging

Going in vivo, including living cells and the whole body, is very important for gaining a better understanding of the mystery of life and requires specialized imaging techniques. The diversity, composition, and temporal–spatial variation of life activities from cells to the whole body require the analysis techniques to be fast-response, noninvasive, highly sensitive, and stable, in situ and in real-time. Functionalized nanoparticle-based fluorescence imaging techniques have the potential to meet such needs through real-time and noninvasive visualization of biological events in vivo.

Functionalized silica nanoparticles (SiNPs) doped with fluorescent dyes appear to be an ideal and flexible platform for developing fluorescence imaging techniques used in living cells and the whole body. We can select and incorporate different dyes inside the silica matrix either noncovalently or covalently. These form the functionalized hybrid SiNPs, which support multiplex labeling and ratiometric sensing in living systems. Since the silica matrix protects dyes from outside quenching and degrading factors, this enhances the photostability and biocompatibility of the SiNP-based probes. This makes them ideal for real-time and long-time tracking. One nanoparticle can encapsulate large numbers of dye molecules, which amplifies their optical signal and temporal–spatial resolution response. Integrating fluorescent dye-doped SiNPs with targeting ligands using various surface modification techniques can greatly improve selective recognition. Along with the endocytosis, functionalized SiNPs can be efficiently internalized into cells for noninvasive localization, assessment, and monitoring. These unique characteristics of functionalized SiNPs substantially support their applications in fluorescence imaging in vivo.

In this Account, we summarize our efforts to develop functionalized dye-doped SiNPs for fluorescence imaging at the cell and small animal levels. We first discuss how to design and construct various functionalized dye-doped SiNPs. Then we describe their properties and imaging applications in cell surface receptor recognition, intracellular labeling, tracking, sensing, and controlled release. Additionally, we have demonstrated the promising application of dye-doped SiNPs as contrast imaging agents for in vivo fluorescence imaging in small animals. We expect these functionalized dye-doped SiNPs to open new opportunities for biological and medical research and applications.

近日，我校化学化工学院王柯敏教授课题组受美国化学会国际著名期刊Accounts of Chemical Research杂志主编Joan Selverstone Valentine教授邀请，撰写了题为“Functionalized Silica Nanoparticles: A Platform for Fluorescence Imaging at the Cell and Small Animal Levels”（Acc. Chem. Res.，**2013, DOI: 10.1021/ar3001525**）的学术论文。

此文总结了王柯敏教授课题组自2000年以来在生物功能化纳米颗粒荧光成像探针设计与制备及其在细胞、亚细胞和小动物活体荧光成像等方面的研究探索。Accounts of Chemical Research杂志在化学研究领域深具影响（**2012年影响因子为21.64**），被认为是化学化工领域顶级综述性杂志之一，主要是综述作者自己的系统研究而不同于其它综述性杂志。

在细胞和活体层面实时、在线、原位地获取与生物功能和疾病相关的生物/化学信息，对于更加准确地阐述疾病发生发展的规律和机制以及实现疾病的早期诊断与治疗等具有十分重要的意义，正逐渐成为现代分析化学的研究热点。然而，细胞和活体层面生命活动的多样性、复杂性和时空多变性等特点，向传统分析方法提出了全新的挑战。二十世纪九十年代以来，纳米技术和生物技术交叉融合发展的纳米生物成像技术为生物活体复杂体系的生物/化学信息获取提供了新的契机。

王柯敏教授近十几年来一直致力于生物/化学信息获取新原理和新方法研究，针对活体复杂体系中生物/化学信息获取必须解决的极小空间、极快响应速度以及超高灵敏度三个关键科学问题，提出了生物功能化纳米颗粒制备、核酸片段传感等系列生物/化学信息获取新原理，在分子、细胞和活体水平系统研究了功能化纳米颗粒生物效应，取得了包括二氧化硅纳米颗粒具有DNase I酶切保护新纳米尺度效应等在内的三项重要科学发现，系统建立了基于生物纳米和分子工程技术的生物/化学信息高灵敏、高选择性以及实时获取新方法，解决了生物/化学信息获取中诸多技术难题，实现了细胞与活体水平生物/化学信息的实时获取与表征，如：设计长Stokes位移近红外荧光纳米探针，克服活体背景荧光干扰，实现了深层组织成像；首次采用金纳米簇实现了肿瘤活体荧光被动靶向成像等。相关研究成果获**2011年国家自然科学二等奖**。

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#早安，湖大# 一个人的“心”再怎么崩裂破碎，“身”还得保持状态，必须健康强壮，支撑起软弱的灵魂。恨是“消耗”，自爱是“补给”。——李碧华（photo by@ze哥）

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