**Responsive nano-biosensor for highly reactive biomarkers monitoring**

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**Introduction:** Rapid advances of chemical and biomedical investigations stimulate the design of new analytical biosensors for precise and accurate sensing and bioimaging of specific disease biomarkers at the subcellular or molecular level.1 These analytical biosensors enable detection and visualisation of the physiological and pathological functions of key biomarkers in live organisms, thus contributing to early diagnosis of diseases and monitoring of their treatments. Of various approaches, optical nano-biosensors that can specifically detect and visualise biomolecules have been recognised as one of the most promising technologies due to their high sensitivity and selectivity in sensing and high spatiotemporal resolution in bioimaging. Nevertheless, conventional molecule and nanoparticle-based sensors for biomarker detection is readily interfered by autofluorescence from complicated biological environments, leading to false positive/negative signals. The short lifetime of disease’s reactive biomarkers (such as reactive oxygen/nitrogen species with less than one second lifetime) necessitates the development of new bioanalytical methods for online detection these unstable and highly reactive biomarkers in situ.

**Methods (Solution):** Accurate detection of these reactive biomarkers are achieved through development of responsive nano-biosensors. The sensor is responsive to a specific reactive biomolecule through a uniquely tailored reaction, leading to proportional optical signal changes for this biomolecule discrimination and quantification.2 The optical output signals can be easily modulated to eliminate the autofluorescence signals *via* three strategies, including anti-Stokes upconversion luminescence,3 time-gated luminescence,4 and photoswitchable “double-checked” luminescence.5 In this abstract, we demonstrate our innovative bioanalytical methods for accurate and background-free detection of reactive biomarkers through description an example of upconversion luminescence nano-biosensor for hypochlorous acid (HOCl) detection.3

**Results and Discussion:** Our recent research led to a new upconversion nano-biosensor for background-free HOCl detection *in vitro* and *in vivo*. This Ru@UCNP nanosensor consists of two functional components, *i.e.* NaYF4: Yb, Tm UCNPs that can convert near infrared (NIR) light to visible light as the energy donor, and a HOCl-responsive ruthenium(II) complex [Ru(bpy)2(DNCH-bpy)](PF6)2 (Ru-DNPH) as the energy acceptor and also the upconversion luminescence (UCL) quencher. Within this luminescence resonance energy transfer (LRET) nanoprobe system, the upconversion luminescence (UCL) OFF-ON emission was triggered specifically by HOCl. This triggering reaction enables the detection of HOCl in aqueous solution and biological systems. As an example of applications, Ru@UCNPs nanoprobe was loaded onto test papers for semi-quantitative HOCl detection without any interference from the background fluorescence. The application of Ru@UCNPs for background-free detection and visualization of HOCl in cells and mice was successfully demonstrated. This research has thus shown that Ru@UCNPs were a selective HOCl-responsive nanoprobe, providing a new way to detecting HOCl and a new strategy to develop novel nanoprobes for in situ detection of various biomarkers in cells and early disgnosis of animal diseases.

**Conclusions:** The successful development of a new NIR-excitable nanoprobe thus provides a robust approach for reactive biomarker detection as well as a new strategy for the design of UCL-based nanoprobe. We will also discuss the other two strategies, including time-gated luminescence and photoswitchable “double-checked” luminescence-based nanosensors in the conference.

**References**

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