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Extended Abstract

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Sensitive and multiplexed response of SERSbased plasmonic nano-dumbbell platforms in disease biomarkers diagnostics

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A rapid, sensitive and accurate response of analytical techniques to resolve health issues, such as low limit identification in special biological environment (i.e. complex mixtures of proteins) remains to being a key aspect in modern proteomics. In fact, extensive efforts to obtain sensitivity enhancements with detection limits even down to the single molecule have been devoted in the nanotechnology framework. Recently, innovative approaches based on the properties of colloidal nanoparticle (NP) assemblies have led to the development of novel diagnostic methods with sensitivity enhancements for single molecule protein monitoring/ identification/detection. Among them, surface-enhanced Raman spectroscopy (SERS) benefits from its higher detectable response to binding of a single protein (sensitivity) and also, very importantly, from its multiplexing capabilities due to the narrow nature of detected peaks from Raman reporter molecules. Since SERS retains the fingerprinting capabilities of Raman spectra, the internal modes of a reporter molecule brought at metallic NPs junctions, where strong field enhancement occurs, can be used as diagnostic tools. Specific attention has been given to SERS-based immunoassays. Indeed, the combination of the high sensitivity provided by SERS and the strong binding specificity of antibody-protein ensures that SERS-based detection platform are suitable tools for biomedical and biochemical analysis, clinical diagnosis and biosensor. Therefore, the superior capabilities of SERS readout strategy such as high sensitivity and simultaneous detection of a multiple proteins in complex matrices will be highlighted in this presentation. Molecular imaging, “the visualization, characterization and measurement of biological processes at the molecular and cellular levels in humans and other living systems”, has gained enormous interest over the last decade. Nanotechnology, an interdisciplinary research field involving physics, chemistry, engineering, biology, and medicine, has great potential for early detection, accurate diagnosis, and personalized treatment of diseases. With the size of many orders of magnitude smaller than human cells, nanoparticles can offer unprecedented interactions with biomolecules both on the surface of and inside the cells, which may revolutionize disease diagnosis and treatment. To date, nanoparticles have been employed in every biomedical imaging modality, including optical imaging, computed tomography, ultrasound, magnetic resonance imaging, single-photon emission computed tomography, and positron emission tomography (PET). The most well-studied nanoparticles for molecular imaging applications include quantum dots (QDs), carbon nanotubes, nanoshells, magnetic nanoparticles, and many others. Among all molecular imaging techniques, no single modality is a perfect fit, with each having its advantages and disadvantages. The fact that Raman spectroscopy can provide molecular/chemical information of the tissue of interest makes it a promising and competitive contender in the molecular imaging arena. Aside from chemical specificity, Raman spectroscopy also possesses many other desirable properties for imaging applications, such as high spatial resolution, superb multiplexing capability, low background signal, and excellent photostability. However, the magnitude of Raman scattering is inherently weak (1 inelastically-scattered photon in every 107 elastically scattered photons) which significantly hampers its biomedical applications. Over the years, several variations of Raman spectroscopy, most notably Coherent anti-Stokes Raman spectroscopy (CARS) and SERS, have been developed to enhance its sensitivity and many in vivo imaging studies with Raman spectroscopy have been successfully achieved. Imaging with SERS has gained significant interest over the last several years. SERS is a plasmonic effect where the molecules adsorbed on a rough metal surface can result in high Raman scattering intensities. Typically, metal nanoparticles (e.g. gold) and various fluorescent dyes (such as Cy3, Cy5, and rhodamine) are used for SERS-based applications.[37] For detailed mechanism of SERS and the design of SERS nanoparticles, interested readers are referred to several excellent recent review articles on this topic. The SERS effect can increase the Raman signal intensity by up to 1014–1015 fold, resulting in a detection sensitivity comparable to fluorescence. To date, a variety of SERS-active nanoparticles, mostly gold- or silver-based, have been conjugated with various targeting ligands (e.g. peptides, proteins, antibodies, antibody fragments, DNA, and Affibodies) for molecular imaging applications. This review article will summarize the current status of molecular imaging with SERS-active nanoparticles. The epidermal growth factor (EGF) and EGF receptor (EGFR) were among the first growth factor ligand-receptor pairs discovered. Subsequently, EGFR was found to be a member of a receptor tyrosine kinase family, the human epidermal growth factor receptor (HER) family. The HER family consists of four closely related members: EGFR (HER1 or ErbB1), HER2 (ErbB2), HER3 (ErbB3), and HER4 (ErbB4). Together, the HER family controls a complex network of ligand-receptor interactions and cellular responses known as the HER-kinase axis. EGFR is a 170 kDa protein which plays a critical role in tumor cell proliferation, differentiation, and survival. EGFR overexpression has been associated with a number of solid tumor types such as head and neck cancer, breast carcinoma, lung cancer, bladder cancer, and colon carcinoma. In addition, EGFR expression is often associated with more aggressive tumors, poor prognosis, and resistance to treatment with cytotoxic agents. Therefore, EGFR is one of the most extensively studied targets in oncology and many monoclonal antibodies (mAbs) have been developed against EGFR for cancer therapy. For SERS-based imaging applications, those that target the EGFR are studied the most extensively, since anti-EGFR mAbs/ligands are widely available.

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